ULTRASOUND EXAMINATION OF THE HEAD AND NECK

ECHOGRAFIE VAN HET HOOFD-HALS GEBIED

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PROEFSCHRIFT

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geboren te Delft

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Overige leden:	Prof. Dr. R.O. van der Heul
	Prof. Dr. H.A. Bruining

To the memory of my father
my mother
Saskia

To Ciska and Sander
my parents

Contents

Both authors accept joint responsibility for the complete contents of this thesis. The Introduction and Part V are written by both authors. R.J. Baatenburg de Jong is primarily responsible for Part II and IV; R.J. Rongen for Part III.

Introduction

Formulation of problems

The fallibility of palpation and current diagnostic tests to detect subclinical (occult) nodal disease in patients with upper aero-digestive tract cancer results in imperfect staging, improper treatment and delayed identification of recurrences in the neck. With continuous advances in imaging techniques (CT, MRI), the sensitivity for the detection of cervical lymph nodes is true enough increasing, while the specificity for detecting metastasis with these techniques remains low. An ideal diagnostic test should be suitable for screening, demonstrating and excluding cervical metastasis. In addition, the test should have no morbidity.

The diagnostic work-up of patients with a head and neck mass is another important diagnostic problem. Although careful history taking and thorough ENT examination may be sufficiently characteristic to permit diagnosis, every clinical diagnosis will be associated with a certain degree of uncertainty. This uncertainty is mainly determined by the limitations of clinical examination in differentiating between solid and cystic lesions on one hand, and the establishment of exact anatomic properties on the other. In addition, there is a proportion of lesions which, despite thorough diagnostic work-up, remain elusive and are subjected to premature surgical exploration. CT may contribute to the pre-treatment work-up but is associated with several important drawbacks: high costs, limited availability, radiation exposure and the need to use intravenous contrast.
A simple, uniformly reliable, non-invasive and cost-effective test would be beneficial in these cases.

The low accuracy of current diagnostic methods in the assessment of cervical nodal disease and the difficulties to evaluate head and neck masses actuated the present study, which started in 1984. By that time small-parts ultrasound transducers had been developed. These high-frequency transducers seemed better suited for examination of the superficial tissues in the head and neck region than earlier ultrasound equipment. In close cooperation between the departments of Radiology and Otorhinolaryngology and Head and Neck Surgery, a prospective study on the value of ultrasound examination of the head and neck was designed. The purpose of this study was to determine the values of palpation and ultrasound examination in the assessment of cervical metastatic disease in patients with upper aero-digestive tract cancer and in the evaluation of head and neck masses. An additional purpose of this study was to appraise the adjunctive value of cytologic examination in the above mentioned clinical problems.

Structure of this thesis

Part I deals with basic bio-physics and bio-effects of clinical ultrasound of the head and neck. Furthermore, the ultrasound anatomy of the head and neck is described and illustrated. In addition, the technique of ultrasound guided fine needle aspiration biopsy (UGFNAB) is outlined.

In **part II** the significance of ultrasound with UGFNAB in the evaluation of the neck of patients with squamous cell carcinoma of the upper aero-digestive tract is outlined. In the comment, possible clinical consequences of ultrasound with UGFNAB in the assessment of cervical node metastasis are formulated.

In **part III** the ultrasound findings in a number of pathologic conditions in the head and neck region are described. In the comment, the value of ultrasound in the evaluation of a head and neck mass is appraised.

In **part IV** an alternative approach to the treatment of deep neck abscesses is presented.

Some general remarks on ultrasound of the head and neck are presented in **part V**.

The chapters II.1 to II.4, the chapters III.1 to III.8, and part IV are edited to be published as papers. Chapter II.1 has been published, part IV is accepted, and the remaining chapters are submitted for publication.

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PART I

Ultrasound of the head and neck

Chapter I.1

Ultrasound imaging principles

Ultrasound is produced by transmitting an electrical current through a piezo-electric crystal in the transducer. This current causes a vibration of the crystal, giving rise to high frequency sound waves which are above the human auditory range. For diagnostic purposes in the head and neck region 5, 7.5 and 10 MHz transducers are used.
The sound waves penetrate the tissues to be examined and are reflected at interfaces of structures with different acoustic impedance. The greater the difference between the impedance of the involved tissues, the stronger will be the returning echo. The echo is picked up by the transducer, transferred into an electrical current and displayed on a screen.
Fluid-filled structures with no internal tissue interfaces appear echo free on ultrasound studies. This results in a black area on the monitor. As a consequence of the low attenuation in a fluid-filled structure, an enhancement is displayed distal to the structure. Solid structures are filled with echoes and appear grey on the screen. Bone reflects rather than transmits sound, resulting in a high density reflection and a posterior acoustic shadowing.
In glandular tissue sound waves are reflected from the multiple acoustic interfaces of parenchyma and stroma.

The resolving power of an ultrasound system is directly proportional to the frequency of the sound waves emitted by the transducer. In other words, the higher the frequency of the sound beam, the smaller the structures that can be identified. Conversely, the higher the frequency, the less the depth of penetration into tissue. Since structures in the neck are relatively superficial, they are well-suited to evaluation by high resolution (high-frequency) ultrasound units, and the limited penetration is of minor importance.
Currently used ultrasound instruments are real-time systems. This means that the reflected ultrasound information is updated numerous times per second. Inherent motion such as vascular pulsation can be appreciated.
The major advantage of real-time systems is their capability to survey a region rapidly and to define a region of interest. Real-time systems incorporate a freeze-frame mechanism to "stop" the moving picture, allowing recording of the image on a film. The illustrations in the next chapters are made in this way. The significance of ultrasonograms on film however, is limited by the fact that ultrasonograms are a reflection of a single moment only in a dynamic study: the observer has no knowledge of the information obtained by the sonographer in previous stages of the ultrasound examination. Furthermore, the exact position of the

transducer relative to the patient is not always clear. These factors interfere with the appreciation of the sonogram by an observer who did not perform the examination himself. Alternatively, selected portions of an examination can be captured on videotape for later reviews.

The ultrasound examinations in this study were performed with an Aloka SSD-650 with UST 5 and UST 7.5 MHz transducers (manufactured by Aloka Co. Ltd., Japan) and a Philips SDR 1500 with 7.5 MHz transducer (manufactured by Philips Ultrasound Inc., Santa Ana, California, U.S.A.).

Chapter I.2

Bio-effects of ultrasound

Ultrasonography is in widespread use in health care because of its proven clinical utility and versatility. An ultrasound investigation is convenient and economical. As with any diagnostic investigation safety is very important in diagnostic ultrasound. In more than thirty years of clinical use there has been no adverse effect reported in diagnostic ultrasound. However, high exposure levels can modify biological structures and functions. There are two major mechanisms producing ultrasound bio-effects, respectively thermal and cavitation mechanisms. Thermal phenomena occur due to the absorption of ultrasonic energy and its conversion to heat. Cavitation involves ultrasonic interactions with small gas bubbles. These bubbles can collapse violently and can produce biological effects in transient cavitation.

Thermal mechanism

By passing through tissues, part of the ultrasound energy is absorbed and converted into heat. In soft tissues and bone, the rise in temperature in the ultrasound beam is less than 1^0C Adverse effects to living mammals from increases in body temperature of 1^0C or less have not been reported. Serious damage may result only from prolonged elevation of the body temperature by 2.5^0C or more.

Cavitation mechanism

The pre-existence of small, stabilized gaseous nuclei is required for acoustic cavitation. Very little is known about their location in mammalian tissues. There is no direct evidence that cavitation causes any biological effects in human subjects under diagnostic conditions.

Epidemiology

Epidemiologic studies and surveys and widespread clinical usage for more than 25 years have yielded no evidence of any adverse effect from diagnostic ultrasound [1 2]. Nonetheless the inability to find convincing proof of an effect, either from epidemiology or from physicians experience, does not preclude the possibility of its happening. Statistical reasoning shows that even with large population studies, it is difficult to identify a small increase in the rate of a commonly occurring event. Subtle effects, long term delayed effects, and certain genetic effects, can easily escape being detected. Therefore, although no negative influences of diagnostic ultrasound are known, ultrasound has to be used carefully on medical grounds, which is expressed in the following official statements on clinical safety of the American Institute of Ultrasound in Medicine[1]:

- No confirmed biological effects on patients or instrument operators caused by exposure at intensities typical of present diagnostic ultrasound instruments have ever been reported. Although the possibility exists that such biological effects may be identified in the future, current data indicate that the benefit to patients of the prudent use of diagnostic ultrasound outweigh the risks, if any, that may be present.

- In those special situations in which examinations are to be carried out for purposes other than direct medical benefit to the individual being examined, the subject should be informed of the anticipated exposure conditions, and of how these compare with conditions for normal diagnostic practice.

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2. Environmental Health Directorate, safety code 23: guidelines for the safe use of ultrasound, part I. Medical and Paramedical Applications, report 8-EHD-59. Ottawa Environmental Health Directorate, 1981

Chapter I.3

Ultrasound features of the head and neck

This chapter deals with general aspects of ultrasound. Furthermore, our findings at ultrasound examination of a normal neck are described.

General considerations on ultrasound imaging

Size of the lesion

Real time ultrasonography permits the sonographer a three dimensional picture of the structures investigated by changing the position of the transducer. As the ultrasound equipment is precisely calibrated, this allows measurement of size in all dimensions.

Localization and relationship of the lesion to adjacent structures

As a result of the three dimensional impression obtained by ultrasound examination the localization and relationship to adjacent structures can be established precisely. Muscular, glandular and vascular structures reveal a clear pattern at ultrasound examination and may serve as a reference point for the localization of a neck mass. Although cartilage, bone and air cannot be visualized by ultrasound, the characteristic reflections caused by these structures may function as a landmark too.

Character of the lesion

The character of a tumor may be solid, cystic or complex (solid and cystic). In distinct cases a solid tumor presents as a low or high echogenic mass, whereas a cyst is echo-free. However, the improvement of ultrasound equipment and the development of high frequency transducers led to an increase of axial and lateral resolution. Cysts, which were formerly depicted as entirely echo-free lesions, nowadays may be visualized as low or high echogenic structures, according to the constitution of the contents. Therefore, although it may seem contradictory, the improvement of small parts transducers may cause problems in differentiation between solid and cystic structures. The solution of this problem may be achieved by special attention to the extent of posterior acoustic enhancement (more explicit in case of a cyst), the visualization of compressibility of the lesion and the depiction of a distinct wall. In case of doubt, aspiration may produce the differentiation between solid and cystic.

Anatomy

Muscular tissue is characterized ultrasonographically by low echogenicity with linear echogenic bands. It can be discerned easily from glandular tissue which reveals a homogeneous parenchymal pattern of high echogenicity. Bone and cartilage produce a strong reflection and posterior acoustic shadowing. Interfaces of tissue and air, as in the oral cavity,

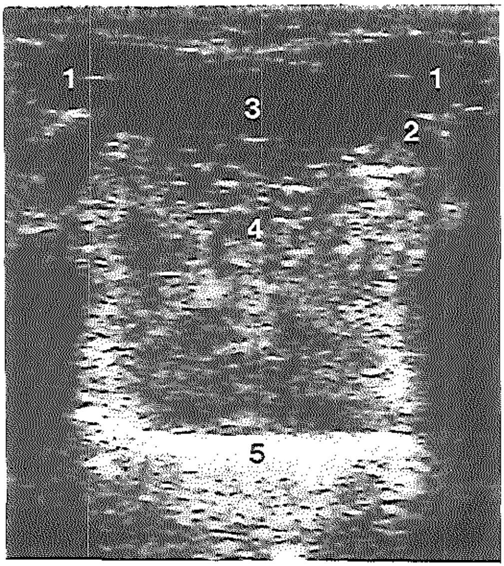

Fig. 1 *Transverse section at the level of the floor of the mouth.*
1. *anterior belly of the digastric muscle*
2. *mylohyoid muscle*
3. *geniohyoid muscle*
4. *genioglossus muscle*
5. *air in the oral cavity*

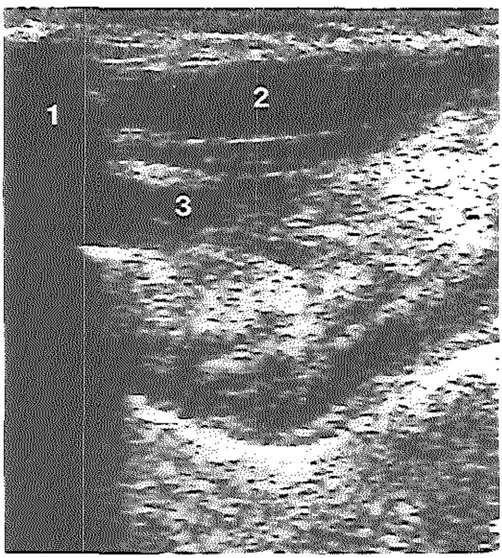

Fig. 2 *Longitudinal section in the midline of the floor of the mouth showing the muscular composition.*
1. *acoustic shadowing of mental spine of mandible*
2. *mylohyoid and geniohyoid muscles*
3. *genioglossus muscle*

pharynx, larynx, oesophagus and trachea, are visualized as strong reflections too.
Depending on the ultrasound properties of adjacent structures, tubular structures (ducts, blood vessels) with a diameter of 2 mm or more may be visualized. Nerves are not visualized by ultrasound.

The floor of the mouth

The floor of the mouth is composed of different muscle layers attached to the mandible and the hyoid bone. The mylohyoid muscles form a diaphragm which is stretched between the left and right halves of the mandible and the body of the hyoid bone. The anterior belly of the digastric muscles is caudal to the mylohyoid muscles. Cranial to the mylohyoid muscles, the geniohyoid muscles are located in the midline. The genioglossus muscle is situated cranial to the geniohyoid muscle (fig. 1). The genioglossus muscles arise from the mental spine of the mandible and fan out in the dorsum of the tongue (fig. 2). Lateral to the genioglossus muscle is the hyoglossus muscle. The styloglossus and palatoglossus muscles cannot be visualized as separate structures.
A longitudinal section posterior to that of fig. 2 shows the base of the tongue (fig. 3).

The submandibular region

The submandibular gland is located lateral and superficial to the digastric muscle. The gland is indented by the mylohyoid muscle, with most of the gland superficial (caudal) to it (fig. 4). The submandibular duct runs along the inferior border of the gland in close relation to the sublingual gland. Because of the constitution of the sublingual glands, which are predominantly mucous with only serous demilunes, these glands are in general difficult to visualize by ultrasound examination. This in contrast to the parotid gland, which is entirely serous in nature. The submandibular gland has serous and mucinous components. In the submandibular region ultrasound examination may also demonstrate the facial artery and vein, and the submandibular lymph nodes.

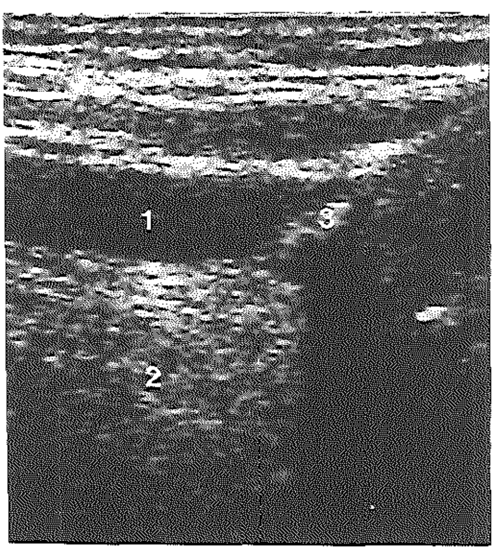

Fig. 3 *Longitudinal section in the midline of the floor of the mouth, dorsal to fig. 2.*
1. muscles of the floor of the mouth
2. base of the tongue
3. hyoid

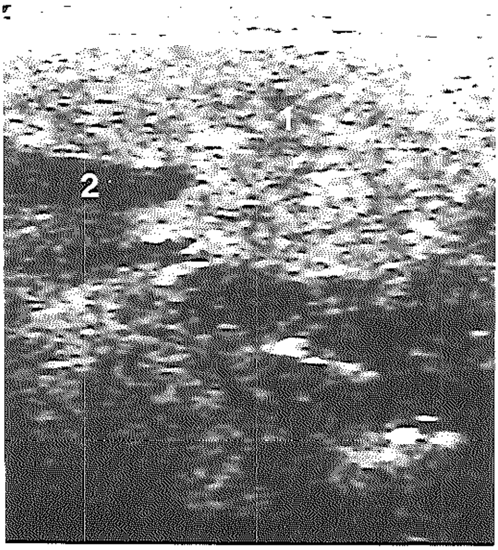

Fig. 4. *Section parallel to the mandible showing the relation of the submandibular gland to the mylohyoid muscle.*
1. submandibular gland
2. mylohyoid muscle

The parotid region

The parotid gland is bounded anteriorly by the mandible and masseteric muscle and posteriorly by the mastoid process, external auditory canal and the sternocleidomastoid and digastric (posterior belly) muscles. The parotid gland is divided into a superficial and a deep lobe. The division is determined by the course of the facial nerve, a structure which cannot

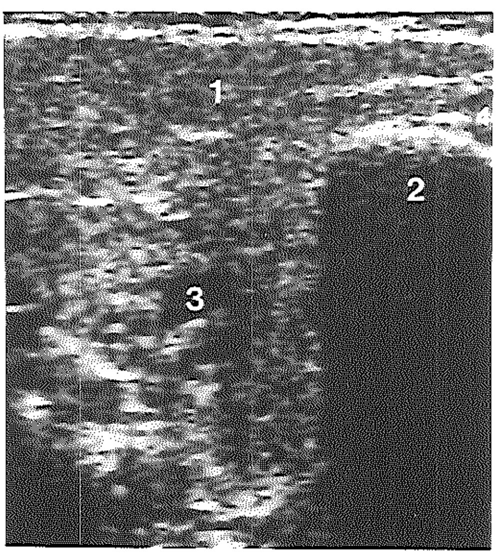

Fig. 5 *Transverse section of the parotid gland at the level of the ramus of the mandible showing the extension superficially to the mandible and the masseteric muscle.*
1. parotid gland
2. acoustic shadowing of the mandible
3. external carotid artery
4. masseteric muscle

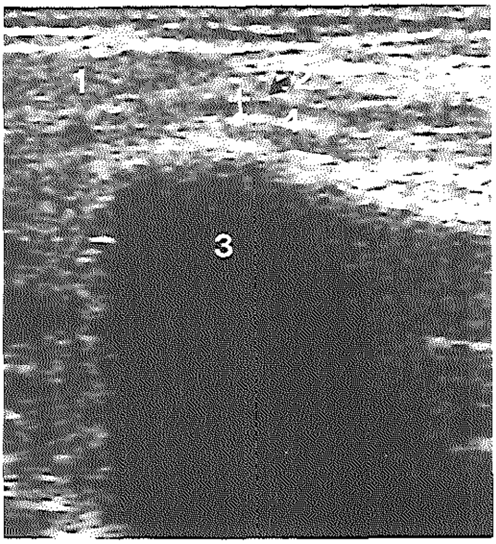

Fig. 6 *Normal parotid duct. Transverse section of the parotid gland at the level of the ramus of the mandible*
1. parotid gland
2. parotid duct
3. acoustic shadowing of the mandible
4. masseteric muscle

be visualized by ultrasound examination. The superficial lobe extends over the masseteric muscle. The deep lobe is situated partly behind the ascending ramus of the mandible (fig. 5). The parotid duct courses anteriorly to the masseteric muscle and opens into the mouth opposite the second upper molar (fig. 6). In general, the parotid duct is depicted only when dilated.
In the parenchymal tissue the external carotid artery (fig. 7), the retromandibular and posterior facial veins can be visualized in most cases.

The lateral neck

The ultrasonically most important structures in the lateral neck are the sternocleidomastoid muscle, the carotid artery, the jugular vein and the lymph nodes (fig. 8, 9). Nodes from 5 mm and above may be visualized.
Differentiation between lymph nodes and muscular tissue may sometimes be difficult, but manipulation with the transducer creates a three-dimensional impression of the structure and gives clarity in most cases.

The thyroid region

The thyroid gland is located in the midline of the infrahyoid neck. The two lobes are connected by the isthmus. Usually, the right lobe is larger than the left lobe. Lateral to both lobes the common carotid artery and the internal jugular vein are situated (fig. 10).
Like the parotid and submandibular glands, the parenchymal tissue of the thyroid gland is characterized by a homogeneous pattern with fine small echoes of equal size.

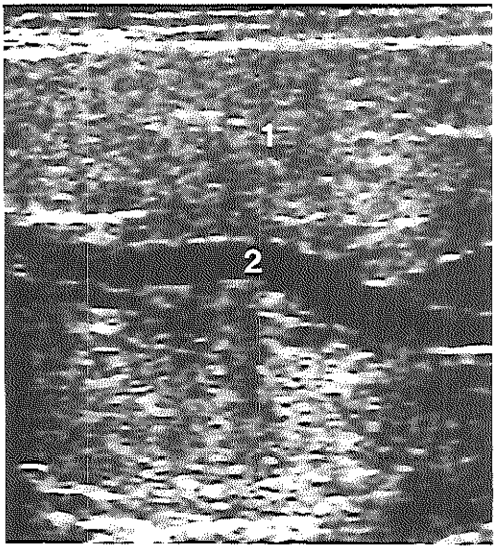

Fig. 7 *Longitudinal section of the parotid gland. The external carotid artery presents as an echo-free tubular structure in the parenchyma of the parotid gland.*
1. parotid gland
2. external carotid artery

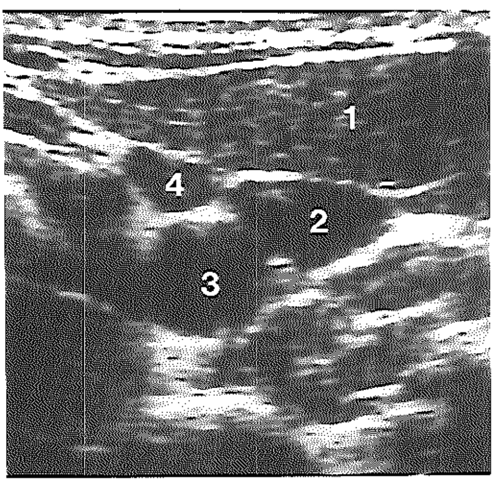

Fig. 8 *Transverse section at the level of the common carotid artery. The internal jugular vein as well as a small lymph node just medial to it are shown.*
1. sternocleidomastoid muscle
2. internal jugular vein
3. common carotid artery
4. lymph node

The parathyroid glands, mostly four in number, are located at the medial dorsal site of each thyroid lobe. The echogenicity is similar to normal thyroid tissue. As a consequence, normal parathyroid glands cannot be distinguished from thyroid tissue. However, parathyroid adenomas may be recognized by a decrease in echogenicity.

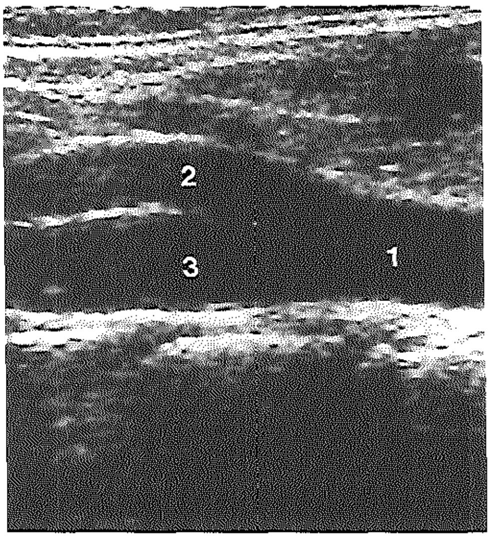

Fig. 9 *Longitudinal section at the level of the carotid artery bifucation.*
1. *common carotid artery*
2. *external carotid artery*
3. *internal carotid artery*

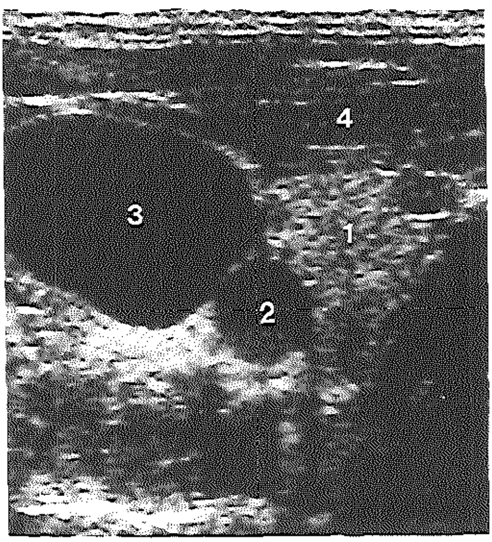

Fig. 10 *Transverse section at the level of the thyroid gland. In comparison to the high echogenic appearance of the glandular tissue of the thyroid gland, the sternocleidomastoid muscle presents as a low echogenic structure with tiny fibrous bands.*
1. *thyroid gland*
2. *common carotid artery*
3. *internal jugular vein during Valsalva manoeuvre*
4. *sternocleidomastoid muscle*

Chapter I.4

Technique of ultrasound guided fine needle aspiration biopsy

Conventional fine needle aspiration biopsy (FNAB) of superficial, palpable masses has been employed successfully for more than 25 years. In the head and neck region FNAB provides an alternative to premature open biopsy of masses in the neck, which is especially ill-advised in case of neck nodes in patients with occult squamous cell carcinoma of the upper aero-digestive tract[1,2]. The risk of tumor seeding in the tract of the needle is negligible[3,4,5].
However, in a considerable number of cases unsatisfactory aspirates are obtained. Review of the literature shows that the percentage of unsatisfactory aspirates varies from 2-14%[6,7,8]. Aspiration of material adjacent to the mass accounts for the majority of non-diagnostic biopsies.
Secondly, with continuous advance of imaging techniques, e.g. ultrasound, the sensitivity for the detection of neck lesions is gradually increasing[9]: lesions with a diameter of 5 mm or more can now be visualized (fig. 1). These non-palpable lesions cannot be examined by conventional FNAB, but require aspiration under ultrasound guidance.
Both the amount of unsatisfactory aspirations with conventional FNAB and the increasing number of neck lesions detected by ultrasound has led us to develop a technique for ultrasound guided fine needle aspiration biopsy (UGFNAB).
During ultrasound guided fine needle aspiration biopsy we use a normal transducer, without an adapter for the needle.
A 0.6 mm needle mounted on a Cameco needle-holder is used. For very small and/or mobile lesions a butterfly needle is used instead. The latter needle allows more subtle manoeuvering and is therefore a valuable alternative for the needle holder.

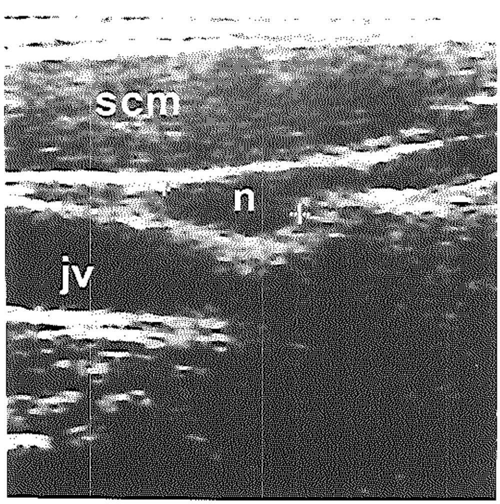

Fig. 1 *Section parallel to the sternocleidomastoid muscle (SCM) showing a small node (N) between sternocleidomastoid muscle and the jugular vein (JV). Cytologic examination of material obtained by UGFNAB showed squamous cell carcinoma.*

Once a mass is visualized it is centered on the monitor, by placing it right under the middle of the transducer (fig. 2). When the lesion is displayed in this way, it is, when necessary, fixed to surrounding tissues by applying gentle pressure with the transducer.
While the sonographer provides optimal imaging, a co-worker introduces the needle into the overlying skin. Depending on the depth of the structure to be examined, the angle between needle and skin can be varied (fig. 3).

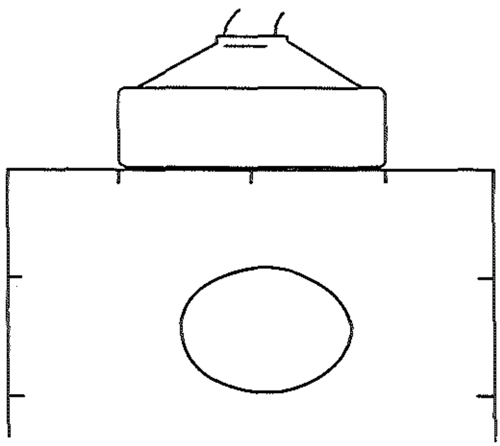

Fig. 2 *Schematic drawing of the position of the transducer: the lesion is placed under the middle of the probe.*

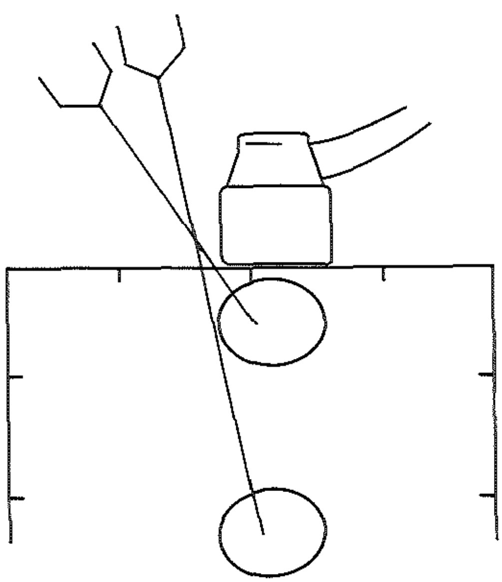

Fig. 3 *Schematic drawing showing that depending on the depth of the lesion to be examined, the angle of the needle with the skin must be adjusted.*

Once the tip of the needle is inside the lesion, it is recognized as a bright, echogenic structure and the plunger of the syringe is retracted, creating a negative pressure in the needle lumen. While a constant vacuum is maintained, the needle is moved back and forth under ultrasound control, and the lesion is sampled in different areas (fig. 4). Subsequently, the plunger is slowly released and the needle withdrawn.
The visibility of the tip reduces the danger of damage to surrounding tissues and ensures that the material is obtained from the lesion to be examined. With ultrasound examination necrotic or cystic areas are distinguishable from solid areas, allowing selective cytologic examination of different parts of a lesion.
We have used this method since 1984 in more than 1000 patients with benign or malignant head and neck pathology. There were no major complications attributable to the aspiration.
The low number of unsatisfactory aspirations (chapter II.2) is striking because most lesions aspirated by UGFNAB were smaller than the lesions that usually are biopsied by conventional FNAB. In conclusion, we recommend our technique for non-palpable lesions in the neck, and for deep, mobile palpable lesions as well.

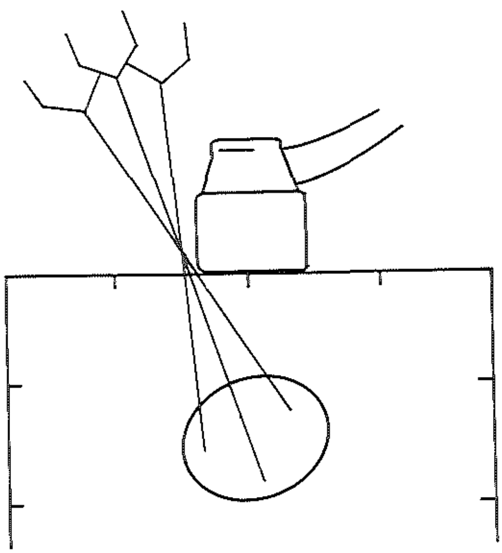

Fig. 4 Schematic drawing illustrating controlled sampling with UGFNAB.

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PART II

Assessment of cervical metastatic disease

Introduction

When this study started in 1984, palpation was the mainstay in the diagnostic work-up of the neck in patients with squamous cell carcinoma of the upper aero-digestive tract. Since most cervical lymph nodes are located superficially, enlarged nodes may be easy to identify. However, small nodes may escape attention, even when palpation is performed by a skilled and experienced head and neck oncologist. Another drawback of palpation is the low specificity of the examination: a considerable proportion of the enlarged cervical nodes appear to be benign at histopathologic examination. Nodal size and extracapsular growth are other features which are inadequately assessed by palpation. Therefore, even expert palpation may be attended by a certain degree of uncertainty on the true status of the cervical lymph nodes. Accordingly, a more accurate diagnostic test is needed.

There were several favourable conditions which led to the development of ultrasound as a diagnostic method in our hospital. Firstly, the presence of an experienced unit for Sonography and the availability of advanced ultrasound equipment. Secondly, the development of small parts transducers improved the possibilities for examination of superficial structures, such as the cervical lymph nodes. Finally, there was long-term experience with head and neck pathology in the department of Cytopathology.

After preliminary experience had shown that it was possible to identify lymph nodes in the neck at ultrasound examination, a prospective study was designed. This study was undertaken to determine the values of expert palpation and ultrasound examination in the assessment of cervical lymph nodes. In addition, the value of cytologic examination of lymph nodes was to be appraised.

Palpation

Expert palpation was to be performed by one of the senior head and neck oncologists (Professor P.C. de Jong, MD, PhD; P. Knegt, MD, PhD; E.J. van der Schans, MD; J.G. van Andel, MD, PhD, and G.J.Gerritsen, MD, PhD). The patients were examined face to face with the examiner, while both were seated. The patient was positioned with his back straight, both feet on the floor with the knees together, his hands relaxed in his lap, and leaning forward just a little. The head of the patient was fixed by placing a hand firmly on top of the head which allowed movement of the head, as constant repositioning is often required. In order to prevent that a region was not included in the examination, a routine order of investigation was used. The submental area was the first to be examined. If this area was under suspicion, a bimanual examination, with the index finger of one hand in the anterior floor of the patients' mouth palpating against the fingers of the opposite hand placed in the submental region, was employed. The hyoid bone and the entire laryngeal skeleton and the thyroid gland were carefully palpated for pre- and paralaryngeal, and paratracheal nodes. The suprasternal notch was examined with the patients' neck in extension. Next the contents of the submandibular triangle were examined; bimanually when indicated. For palpation of the jugular nodes on one side of the neck, the patients' head was rotated slightly to the opposite side and flexed, to allow relaxation of the overlying sternocleidomastoid muscle. The jugular nodes were examined between the thumb and index finger of the examiner. The supraclavicular region was examined with the flat surface of the fingers, both during flexion and during slight extension of the patients' neck. The posterior triangle of the neck was examined with the flat surface of the fingers, while the patient's neck was slightly flexed to the side to be examined. Finally, the pre-auricular region was scrutinized for lymph nodes with the flat surface of the fingers. Size, number, location and characteristics of nodes were recorded in a diagram (Appendix A).

Ultrasound examination and UGFNAB

Firstly, it was necessary to explore the complex anatomy of the head and neck region. Secondly, for the optimal use of the ultrasound equipment which was available, experience had to be gained. Gradually, knowledge of the ultrasound appearance of the structures in the head and neck (chapter I.3), and experience in the use of the equipment, increased. Since it appeared that most regions of the neck at risk for cervical node metastases could be visualized, a standardized ultrasound examination of the neck could be developed. The examination included: the submental, submandibular, buccal, pre-auricular, jugulo-digastric, retromandibular, posterior cervical, supraclavicular, and anterior regions of the neck, and the parapharyngeal space. Due to the presence of bony structures (cervical spine) and the air in the pharynx, the retropharyngeal nodes could not be visualized.
Because of the low incidence of nodal metastasis in the naso-labial, suboccipital and retro-auricular regions, these regions were excluded from the routine examination.
Initially, the investigation of the neck took 20-30 minutes. During the course of the study, the time necessary for a complete examination decreased to 10-15 minutes.
At first, adapters for a needle holder were used during UGFNAB. This proved to be very laborious, and gradually the technique as described in chapter I.4 was developed. After some experience was acquired, this technique appeared to be quite efficacious, taking only a few minutes for each node to be examined.
It was impossible to make arrangements for the presence of a cytopathologist during the ultrasound examination. Therefore, special attention was given to the preparation of the smears by the sonographer. Following aspiration, the syringe and the needle were detached from one another and the syringe was filled with air and reattached to the needle. Subsequently, the needle was placed in contact with a clean, dry, glass slide and a droplet of the aspirate was deposited at one end of a glass slide and then pulled to the other end by

another slide (held at 45^0) in a way that the material was feathered out. If there was sufficient material, some of it was transferred to another slide. Subsequently, the smear was air-dried and sent to the department of Cytopathology.
UGFNAB required a diameter of the lesion of at least 5 mm, preferably more than 7 or 8 mm (chapter I.4). In the view of the load on the patient, efficiency, costs and the limited value of the information obtained by aspirating more than two nodes, the number of UGFNABs on one side of the neck was limited to two. In case of multiple node involvement on one side of the neck, only the most cranial and most caudal nodes were aspirated. When these nodes were relatively small, or when a conglomerate nodal mass was depicted, the largest node was aspirated.
Initially, cytologic examination of palpable nodes was often performed by the oncologist. When an UGFNAB of depicted nodes was indicated, the patient was asked whether there was an aspiration performed by the head and neck oncologist before. If so, the aspiration was not repeated. During the study it became customary that all aspirations were performed with ultrasound guidance.
Until October 1987, the ultrasound examinations and UGFNABs were performed by the authors, and, in case of absence, by the head of the department of Ultrasound J.S.Lameris (JSL). During the remaining period of the study, the examinations were performed by a resident with special interests in sonography (H. van Overhagen, MD (HvO)), and JSL.
The presence of a malignant tumor in the head and neck region was the only clinical information available for the sonographer; neither location and T-stage of the primary tumor, nor information on the clinical status of the cervical nodes were mentioned.
Findings regarding size, location, relationship to surrounding structures, ultrasound characteristics and exact location of the nodes which were aspirated were recorded in a diagram (Appendix A).
Although care was taken that the individual ultrasound examinations were performed without knowledge of clinical data, there was an extensive feed-back through communication between the two authors, one being a radiologist, and the other a clinical physician. When a final diagnosis was available, or when the results of the cytologic examination were known, the findings of the sonographer were reviewed in light of the clinical and diagnostic data.

Cytopathology

During our study, the May-Gruenwald-Giemsa stain for air-dried material was used. The smears were examined by a cytopathologist (D.I.Blonk, MD, PhD; R. van Pel, MD, PhD), and classified according to Papanicolaou. Because there is a gradual transition between the stages I-V, reliable differentiation is difficult and requires dedication and experience. The Papanicolaou classification for squamous cell carcinoma in cervical lymph nodes is based on the presence of epithelial cells, the size, shape and appearance of the nuclei, the presence of nucleoli, and the number of deviant epithelial cells. The accuracy of cytologic examination in the University Hospital Rotterdam is discussed in chapter II.2.

Histopathologic examination

Histopathologic examination of neck dissection specimens (supplied with perioperative findings when necessary) was the gold standard of diagnosis in the studies described in chapters II.1, II.2 and II.3.

Neck dissection was performed less than 3 weeks after palpation and ultrasound examination. The specimens were preserved in a formaldehyde solution. Histopathologic examination was conducted by one of the senior pathologists in the University Hospital Rotterdam according a standard procedure. Macroscopically enlarged nodes were removed and sectioned. Furthermore, specimens were sliced at 3 to 4 mm intervals. These intervals were given a number which was indicated on an instant photograph of the specimen. In this way the location of the nodes could be reflected in the histopathological report. The findings at palpation, sonography and cytologic examination were compared with the data in the histopathological reports and instant photographs.

Selection of the patients for this study

From December 1984 until December 1988, approximately 1500 ultrasound examinations of the neck were performed for cervical nodal disease. Only a fraction of these patients are included in this study. For several reasons, the majority of the 1500 patients was excluded. Firstly, because the findings of the oncologist were not recorded, or were recorded incompletely and did not allow comparison with the findings at ultrasound examination and/or histopathologic examination. Secondly, during the course of the study, more and more patients were referred for ultrasound examination of the neck by physicians from other departments. These patients were patients with non-epithelial malignancies, or patients with squamous cell carcinoma outside the head and neck region. Later on, patients with upper aero-digestive tract cancer were sent from neighbouring hospitals for ultrasound evaluation of the neck. All these patients were excluded from our study.

A minority of the patients was not included because the ultrasound examination was performed by a radiologist who was not one of the investigators in this study. Finally, many cases had to be excluded because there was no proper verification of the findings: e.g., many patients were suspected to have lymphadenopathy, whereas ultrasound demonstrated no abnormalities at all, an enlarged submandibular gland, a large and caudally placed tail of the parotid gland, the transverse process of the first cervical vertebra, etc. These patients were excluded because no gold standard of comparison was available. The remaining patients entered the study. These patients included new patients presenting with squamous cell carcinoma of the upper aero-digestive tract; patients with a recurrence of the primary tumor;

patients with a (suspected) relapse in the neck and patients in whom the effect of chemo- and/or radiotherapy was evaluated.

The purpose of the study was to evaluate the value of palpation and ultrasound examination in the assessment of cervical lymph node metastases. In the assessment of cervical nodal disease, a reliable differentiation between necks with and without metastatic involvement is one of the most important issues. The values of palpation, ultrasound examination, and ultrasound with cytologic examination in this respect were studied in chapter II.1. In chapter II.2, the efficacy of UGFNAB is compared to the efficacy of FNAB. Furthermore, the value of the cytologic examination was compared to the data available in relevant literature. Chapter II.3 deals with the evaluation of the number and level of cervical metastasis by palpation, CT and ultrasound examination. In addition, the evaluation of other important parameters of cervical metastatic disease (size and extra-nodal spread) is discussed. The values and limitations of palpation, ultrasound and CT in the assessment of nodal disease are outlined, and the place of these diagnostic methods in the diagnostic work-up is defined.
In chapter II.4, the previously demonstrated properties of palpation, and ultrasound with cytologic examination are applied to 200 consecutive patients presenting with squamous cell carcinoma of the upper aero-digestive tract. This is to illustrate how the use of ultrasound with cytologic examination may affect current staging.
In chapter II.5 the possible consequences of applying ultrasound with UGFNAB on the clinical management of patients with squamous cell carcinoma of the upper aero-digestive tract are discussed.

Chapter II.1

Metastatic neck disease; palpation versus ultrasound examination

A clinical - radiographic - histopathologic prospective study.

(As published in Arch. Otolaryngol. Head and Neck Surgery 1989; 115: 689-690. Revised for this thesis).

Abstract

Nodal disease is a diagnostic problem in head and neck oncology. Current methods for investigation of the neck are not satisfactory as far as differentiation between necks with and without metastatic involvement is concerned. In the present study, the results of palpation and ultrasound examination were compared with histopathologic examination results of 120 neck dissection specimens. Furthermore, the value of ultrasound examination combined with cytologic examination of neck nodes was evaluated.
Ultrasound examination was characterized by a high sensitivity of 96.8% and specificity was 32.0%. When the results of ultrasound guided fine needle aspiration biopsy were added to the ultrasound findings, the sensitivity-rate was not changed. However, specificity appeared to be as high as 92.9%. From these results it is concluded that ultrasound with fine needle aspiration biopsy is an accurate method for assessment of the neck in head and neck oncology.

Introduction

Treatment and prognosis of patients with head and neck neoplasms are mainly determined by nodal disease. Differentiation between necks with and without metastatic involvement, however, is still a diagnostic problem in head and neck oncology. Current methods for investigation of the neck are not satisfactory as both palpation and computed tomography are characterized by high false negative and false positive rates.
Reviewing relevant literature, it can be stated that palpation has a false negative rate between 15 and 65% (most authors mention 25%) and a false positive rate between 10 and 15%[1 2 3 4]. In a recent article by Feinmesser et al.[5] the false positive rate of computed tomography was 18.4% and the false negative rate was 34%. In this study, no significant differences in the false positive and false negative rates were demonstrated for palpation and CT. Low specificity and other drawbacks of CT (the need for using intravenous contrast medium, radiation exposure and relative high costs), have led us to test ultrasound examination as an alternative imaging modality for investigation of the neck. Results of a pilot study were recently published[6]. The present study was undertaken to compare palpation, ultrasound and histopathologic findings. Furthermore, the value of fine needle aspiration biopsy for

cytologic study of neck nodes in combination with ultrasound examination is evaluated.

Patients and methods

Between December 1984 and April 1988, 100 patients with head and neck cancer were, before neck dissection, examined by palpation of the neck and ultrasound examination. With few exceptions the neoplasms were squamous cell carcinomas. Sixty-two necks were treated by radiotherapy before they entered the study.

All patients were examined by one of the members of the oncological staff. Size and localization of palpable nodes were documented (Appendix A).

Subsequently, patients were referred to the radiology department. The ultrasound examination was performed by RJR, RJBdJ, JSL or HvO, without any knowledge of the previous clinical observations of the oncologist.

In 84 necks fine needle aspiration biopsy was done under ultrasound guidance after preliminary experience had demonstrated that nodes larger than 5 mm could be aspirated by using this technique. In case of multiple nodes, the most cranial and most caudal nodes were aspirated.

The 100 patients included in this study underwent 120 neck dissections. Neck dissection was performed less than 3 weeks after clinical and ultrasound examinations. Unilateral dissection was of the radical type (in most cases, the spinal accessory nerve was preserved). In case of bilateral dissection, one side was of the radical type and the opposite side was of the modified type. Neck dissection specimens were preserved in a formaldehyde solution and examined by a senior pathologist. Macroscopically enlarged nodes were removed and sectioned for histopathologic investigation. Furthermore, the specimens were sliced at 3 to 4 mm intervals.

Results

Palpation, ultrasound and histopathologic findings.

In 95 neck dissection specimens, one or more metastases were demonstrated by histopathologic examination. Palpation correctly identified one or more metastases in 70 necks, whereas ultrasound depicted one or more metastases in 92 necks. False negative rates were 25 for palpation and 3 for ultrasound examination.

In 25 neck dissection specimens, no metastases were found on histopathologic examination. From these, 15 were correctly identified by palpation; 8 were correctly assessed by ultrasound examination. In 10 necks, one or more nodes were found on palpation; these later appeared to be benign (10 false positive results). Ultrasound examination detected one or more benign nodes in 17 necks (17 false positive results).

No palpable nodes were missed by the ultrasound investigation. Furthermore, histopathologic examination demonstrated 20 to 40 small, benign nodes in each surgical specimen. Ultrasound examination and palpation often failed to demonstrate these smaller

Table 1: Test characteristics of palpation, ultrasound examination and combined procedure (ultrasound with cytologic examination).

	SENS	SPEC	PPV	NPV	ACC	PREV
PALPATION (n=120)	73.3	60.0	87.5	37.5	70.8	79.2
ULTRASOUND EXAMINATION (n=120)	96.8	32.0	84.4	72.7	83.3	79.2
ULTRASOUND EXAMINATION WITH CYTOLOGY (n=84)	95.7	92.9	98.5	81.3	95.2	83.3

SENS = Sensitivity: ability of the test to detect the disease when it is present
SPEC = Specificity: ability of the test to identify the absence of disease
PPV = Positive predictive value: probability that necks diagnosed as having neck disease will indeed have metastatic involvement
NPV = Negative predictive value: probability of disease being absent when the test result is negative
ACC = Accuracy: overall agreement between the test and the gold standard
PREV = Prevalence: proportion of the truly diseased individuals to whom the test was applied

The differences between the sensitivity and specificity of ultrasound examination and palpation are statistically significant (two-sided p-value less than .001 and less than .05, respectively, by McNemar' s test).

nodes. The smallest metastasis detected by ultrasound measured 5 mm in diameter.
In 3 of 100 patients, both ultrasound examination and palpation failed to demonstrate metastatic disease. The missed nodes measured 9, 15, and 20 mm. These nodes were localized in the jugulodigastric (1 node) and low jugular (2 nodes) regions. Two of the nodes ultrasound examination had failed to detect were in necks which were not irradiated.
The test-characteristics of palpation, ultrasound, and ultrasound with cytologic examination are presented in Table 1.

There was a slight difference in the sensitivity-rates of palpation and ultrasound examination between irradiated necks, and necks which were not irradiated (Table 2). The differences were not statistically significant.

Ultrasound, cytologic and histopathologic findings.

In 84 necks, lymph nodes demonstrated by ultrasound examination were aspirated for cytologic examination. The results of this procedure were compared with histopathologic

Table 2 The sensitivity-rates of palpation and ultrasound examination for the detection of metastatic disease in necks which were irradiated, and necks which were not irradiated. One hundred-and-twenty necks were examined; 62 were irradiated, the remaining 58 necks were not.

	SENSITIVITY PALPATION	SENSITIVITY ULTRASOUND
IRRADIATED	76%	98%
NON-IRRADIATED	71%	96%

examination results. Of the 84 necks, 70 had one or more metastases. Sixty-seven of these 70 necks were correctly diagnosed by the combination of the results of ultrasound and cytologic examination. Ultrasound examination failed to demonstrate cervical lymph node metastases in the remaining 3 necks.

Thirteen necks contained reactive nodes only; these were demonstrated by ultrasound examination and fine needle aspiration biopsy and confirmed by histologic examination. One cytologic examination appeared to yield a false positive result.

Discussion

Imaging today plays an important role in the evaluation of disease in the cervical lymph nodes and should be part of any thorough work-up of patients with head and neck cancer[7]. Continuous advance of techniques leads to increasing sensitivity of the imaging modalities in the detection of lymph nodes. However, differentiation between benign nodes and nodes with metastatic involvement is not possible as far as ultrasound examination, CT and magnetic resonance imaging (MRI) are concerned. Although several criteria have been developed for this purpose, specificity of all imaging modalities is low. Moreover, increasing sensitivity for detection of nodes inevitably leads to decreasing specificity for metastatic disease.

In our study, the ultrasound examination was characterized by high sensitivity (96.8%) when compared with palpation (73.7%); specificity of both examinations was low (32.0% for ultrasound and 60.0% for palpation) (Table 1).

Although the sensitivity of the ultrasound examination was high, the major advantage of ultrasound examination is that it is, unlike CT and MRI, easily combined with fine needle aspiration cytology. This procedure only takes a few minutes for each node, while biopsy under guidance of CT or MRI is timeconsuming and costly. The specificity of the combined results of ultrasound and cytologic examination was significantly higher than palpation or ultrasound examination alone: 92.9% compared with 60.0% and 32.0% respectively (Table 1).

The positive predictive value (Table 1) of the combined procedure was 98.5%, indicating

that there is a high probability that necks diagnosed as having neck disease will indeed have metastatic involvement. The negative predictive value (the probability of a disease being absent if a test result is negative) was 81.3% (Table 1). The overall agreement between ultrasound examination with fine needle aspiration biopsy and the golden standard (histopathologic study) was 95.2% (Table 1).
No statistically different sensitivity-rates rates of ultrasound were found for irradiated and non-irradiated necks. This may be caused by the size of the metastases, which is, in our experience, larger in case of a relapse after previous treatment.
During, or shortly after irradiation, ultrasound examination may be hampered by edema in the subcutaneous tissues. When pronounced, the edema gives rise to reflections which may disturb the assessment of deep structures. However, when ultrasound examination is performed during follow-up when the edema is resolved, the changes in ultrasound appearance of the structures in the head and neck region are mostly of little importance, or absent.

Conclusion

Ultrasound examination combined with fine needle aspiration biopsy, is an accurate method for assessment of the neck in head and neck oncology, and may be used for screening, demonstrating, and excluding cervical metastases.

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Chapter II.2

Ultrasound guided fine needle aspiration biopsy of neck nodes versus conventional fine needle aspiration biopsy

Abstract

The sensitivity of ultrasound examination for detection of neck nodes is high; the specificity for metastases however, is low. In order to establish its place in the evaluation of patients with squamous cell carcinoma of the upper aero-digestive tract, the value of ultrasound guided fine needle aspiration biopsy (UGFNAB) was studied and compared to conventional fine needle aspiration biopsy (FNAB). Histopathologic examination was the gold standard of this study. All statistical characteristics of UGFNAB appeared to be superior to conventional FNAB. Furthermore, although nodes examined by UGFNAB were generally smaller and non-palpable, UGFNAB was characterized by less non-diagnostic aspirations. It is concluded that UGFNAB is a reliable technique for differentiation between benign nodes and cervical lymph node metastases and therefore adds important information to the value of ultrasound examination.

Introduction

In patients with squamous cell carcinoma of the upper aero-digestive tract, cytologic examination of neck nodes is a frequently used method to distinguish between benign and malignant disease. Frable and Frable[1] note a 95% sensitivity for the presence of tumor in palpable cervical nodes and a 98% specificity for the absence of malignancy. These and other authors[2 3 4 5] report an accuracy of conventional fine needle aspiration biopsy (FNAB) varying from 80 to 98%.

With the introduction of small-parts transducers for ultrasound equipment many non-palpable lesions are visualized[6 7], (chapter II.1). In order to allow differentiation between benign nodes and cervical lymph node metastases, these lesions require cytologic evaluation by fine needle aspiration biopsy, which is necessarily performed under ultrasound guidance: ultrasound guided fine needle aspiration biopsy (UGFNAB) (chapter II.4). In this retrospective study, the results of cytologic examination of material obtained by UGFNAB are compared with cytologic examination of material from palpable nodes obtained by FNAB. Histopathologic examination of subsequently performed radical neck dissection was the gold standard of this study.

Patients and methods

Between January 1980 and January 1988, 143 cervical nodes of patients with squamous cell carcinoma of the upper aero-digestive tract were examined cytologically prior to (radical) neck dissection. From 1980 until 1985 FNAB only was performed (36 cases); from 1985 onwards both FNAB (31 cases), and UGFNAB (76 cases) were employed.

FNAB technique

The well-known FNAB technique described by Frable and Frable[1] was applied, using the Cameco syringe-pistol with a 20 ml disposable syringe and a 0.6 mm needle. FNAB was performed by a head and neck oncologist, or by a cytopathologist.

UGFNAB technique

Lymph nodes were visualized by ultrasound examination with small-parts transducers. For aspiration, the above described FNAB technique was modified by the continuous monitoring of the tip of the needle by ultrasound (chapter II.4). UGFNAB was performed by RJR, RJBdJ, JSL or HvO.

Smear preparation

Thin smears from the aspirated material were air-dried and stained with May-Grünwald-Giemsa staining methods.

Cytologic examination

All smears were examined by an experienced cytopathologist. Samples were classified according to Papanicolaou. Retrospectively, Pap I and II were considered benign (negative) and Pap IV and V malignant (positive). A smear classified as Pap III was considered as being a non-diagnostic aspirate.

Histopathologic examination

The neck dissection specimens were preserved in a formaldehyde solution and examined by a senior pathologist. Macroscopically enlarged nodes were removed and sectioned for histopathologic examination. Furthermore, the specimens were sliced at 3 to 4 mm intervals.

Results

FNAB (67 cases) was characterized by 38 true positive, 14 true negative, 3 false positive and 5 false negative results (Table 1). In 7 cases no satisfactory diagnosis could be made because the aspirate did not contain lymphatic or epithelial cells (6 smears) or was classified as Pap III (1 smear). The test characteristics of FNAB are shown in Table 2: sensitivity 88%, specificity 82%, positive predictive value 93%, negative predictive value 74% and accuracy 87%.

The results of 76 UGFNABs can be specified as follows: 55 true positive, 18 true negative, 1 false positive and 1 false negative cytologic examinations. In 1 smear only blood and muscle cells were observed; the sample was considered not satisfactory (Table 1). From these data

Table 1a Results of FNAB compared to histopathologic examination

	HIST+	HIST−
FNAB+	38	3
FNAB−	5	14

Unsatisfactory for interpretation: 7

Table 1b Results of UGFNAB compared to histopathologic examination

	HIST+	HIST−
UGFNAB+	55	1
UGFNAB−	1	18

Unsatisfactory for interpretation: 1

Table 2 Test-characteristics of FNAB, UGFNAB and FNAB + UGFNAB

	FNAB	UGFNAB	FNAB + UGFNAB
SENSITIVITY	88%	98%	94%
SPECIFICITY	82%	95%	89%
PPV	93%	98%	96%
NPV	74%	95%	84%
ACCURACY	87%	97%	93%
NO DIAGNOSIS	10%	1%	5%
PREVALENCE	72%	75%	73%

the following test characteristics were calculated: 98% sensitivity, 95% specificity, 98% positive predictive value, 95% negative predictive value and 97% accuracy (Table 2).

The over-all results of cytologic examination (FNAB and UGFNAB) were characterized by 94% sensitivity, 89% specificity, 96% positive predictive value, 84% negative predictive value and 93% accuracy. In 5% of the aspirates no diagnosis could be made (Table 2).

There were no complications attributable to the aspiration.

Discussion

With continuous improvements of CT, MRI and ultrasound, the sensitivity of imaging techniques for detection of neck nodes is gradually increasing. As it remains difficult to identify benign and metastatic disease on grounds of radiologic characteristics only, tissue diagnosis would be beneficial. However, it is well established that open neck biopsy in case of squamous cell carcinoma of the upper aero-digestive tract is detrimental[8]. Cytologic examination may provide important additional information instead: cytologic examination of palpable nodes has proven to be an accurate method for differentiation between benign nodes and cervical lymph node metastases[1 2 3 4 5]. No serious side effects of FNAB have been reported[2 9].

In relevant literature, the value of a positive cytologic diagnosis of metastatic disease is undisputed. In our study however, 4 false positive results were noted in 143 examined nodes. These nodes were classified as Pap IV (3 cases; 2 FNAB, 1 UGFNAB) and Pap V (1 FNAB). All nodes were present in previously irradiated necks and appeared to be necrotic on histopathologic examination. There were no false positive results from nodes which were not irradiated.

UGFNAB was characterized by less false negative results and less non-diagnostic aspirations than FNAB. These differences are probably due to the continuous monitoring of the tip of the needle and the node during UGFNAB, which allows controlled sampling from different areas within a node, reducing the chance of leaving a part of a node unexamined. The number of non-diagnostic aspirations may also have been influenced by the fact that patients were selected for this study on the basis of the availability of the results of histopathologic examination. When the result of cytologic examination is non-diagnostic, the patient was less likely to be referred for the gold standard procedure. Therefore, in every day clinical practice, the number of non-diagnostic aspirations can be expected to be higher.

In view of the low number of false negative results of UGFNAB and the test parameters of cytologic exmination which are reported in literature[1 2 3 4 5 9 10], the value of a negative cytologic diagnosis should be reconsidered: usually, palpable nodes are considered metastatically involved, irrespective of the outcome of cytologic examination. Our results however, indicate once more that there is a high probability that nodes with a negative result on (UG)FNAB indeed are benign on histopathologic examination.

Considering the fact that nodes aspirated under ultrasound guidance were generally non-palpable and usually smaller than the nodes aspirated in the conventional way, our results indicate that UGFNAB is more efficient than FNAB: in only 1 case out of 76 UGFNABs no diagnosis could be made; conventional FNAB yielded non-satisfactory material in 10% of the aspirations. It is assumed that the sampling technique is responsible for the more advantageous results of UGFNAB when compared to FNAB.

The results of FNAB in this study seem to compare unfavourable with those of other authors[1-5]. However, most of our false negative results (4 of 5) were noted in the first years after introduction of FNAB in our institution. Furthermore, irradiation accounted for all false positive results, whereas in other studies, irradiated nodes were not included or previous irradiation was not mentioned. Therefore, our results may not be as unfavourable as they seem.

Conclusions

In patients with squamous cell carcinoma of the upper aero-digestive tract:

1. UGFNAB is (at least) as accurate as conventional FNAB.
2. UGFNAB permits cytologic examination of non-palpable lymph nodes.
3. False positive cytologic examinations only occur in nodes which are previously irradiated.
4. High sensitivity, high specificity and high negative predictive value of UGFNAB indicate that a negative diagnosis of UGFNAB excludes metastatic involvement with a high degree of reliability.
5. Our results demonstrate once more that cytologic examination, when performed by a well-trained team of a cytopathologist and a clinician or sonographer, is an accurate technique for differentiation between benign nodes and cervical lymph node metastases.

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Chapter II.3

Assessment of cervical metastatic disease by palpation, ultrasound examination and CT

Abstract

The purpose of this study was to establish the significance of palpation, ultrasound examination and CT in the assessment of the status of cervical nodes. In 36 patients with upper aero-digestive tract cancer, the results of these diagnostic tests were compared to the results of histopathologic examination of neck dissection specimens. Ultrasound proved to compare favourably to the other tests with regard to the sensitivity for the detection of nodal metastases and to the establishment of multiplicity of metastases. The sensitivity-rates for detection of patients with metastatic involvement did not differ as far as CT and ultrasound were concerned.

The values and limitations of palpation, ultrasound examination and CT in the assessment of nodal metastases with respect to size, number, localization and extra-nodal tumor spread are discussed, and a place for these tests in the diagnostic work-up is defined.

Introduction

Prognostic factors of upper aero-digestive tract cancer include the presence of metastases, their size, number, level/localization and the presence of extra-nodal spread. These factors cannot be adequately assessed by palpation of the neck[1 2 3 4] and therefore imaging techniques are advocated. In chapter II.1, high sensitivity and specificity of ultrasound with ultrasound guided fine needle aspiration biopsy (UGFNAB) in discriminating between necks with or without metastatic involvement were established. The objective of the present study is to compare the values of palpation, ultrasound examination and CT with regard to the presence or absence of nodal disease and to the number of involved nodes. Furthermore, the value of each technique at the different levels of the neck is assessed in order to define their precise indications.

Patients and methods

Between December 1984 and December 1988, all patients with squamous cell carcinoma of the upper aero-digestive tract were, before neck dissection, examined by palpation and ultrasound of the neck. In 36 patients CT of the neck was performed as well. These 36 patients are the subject of this study.

<u>Palpation</u> (n=36)

All patients were examined by a member of the oncological staff. Size, number and localization of palpable nodes were recorded in a diagram (Appendix A).

Ultrasound (n=36)

Ultrasound examination was performed without knowledge of the results of palpation. Size, number and localization of depicted nodes were recorded (Appendix A).

CT (n=36)

From the mastoid process to the thoracic inlet, 6 mm contiguous axial scans were made. Intravenous contrast medium was administered in all patients. Scans were independently and retrospectively reviewed by RJR, and size, number and localization of nodes were recorded (Appendix A). No attempt was made to differentiate between reactive nodes and metastases on the basis of nodal size and/or morphoradiologic criteria: all visible nodes were regarded as being metastases.
CT was performed with a Philips Tomoscan 350.

Histopathologic examination

Neck dissection was performed less than 3 weeks after palpation, ultrasound examination and CT. In the 36 patients, 44 neck dissections were performed (28 unilateral and 8 bilateral dissections). Unilateral dissection was of the radical type (with preservation of the spinal accessory nerve in most cases). In case of bilateral dissection, the internal jugular vein was preserved on one side. Neck dissection specimens were examined by a senior pathologist. Macroscopically enlarged nodes were removed and sectioned for histopathologic investigation. Furthermore, the specimens were sliced at 3 to 4 mm intervals; macroscopically suspect areas were also sectioned.
While reviewing the reports of the histopathologic examination, it proved to be impossible to distinguish between nodes in the low jugular and low posterior cervical region. Therefore, these nodes were referred to as lower cervical nodes. Besides, it appeared that the number of reactive nodes which were found was not recorded in all cases. As a result, true negative rates for single nodes are not available.

Results

Patients (Table 1a)

Thirty-one patients had metastases at one or both sides of the neck. Twenty-five patients were identified as having metastatic involvement by palpation. In 30 patients metastases were found at ultrasound examination and CT.

Table 1a Results of palpation, ultrasound examination and CT in the assessment of cervical metastatic disease in 36 patients with squamous cell carcinoma of the upper aero-digestive tract. In this table, positive applies to patients with nodal metastases, and negative to patients without nodal involvement.

Palpation

	Metastases	No metastases
Positive	26	2
Negative	5	3
	31	5

Sensitivity of palpation: 84%

Ultrasound

	Metastases	No metastases
Positive	30	4
Negative	1	1
	31	5

Sensitivity of ultrasound: 97%

CT

	Metastases	No metastases
Positive	30	2
Negative	1	3
	31	5

Sensitivity of CT: 97%

The differences between the results of palpation, ultrasound and CT are not significant (double sided p-value .12) (sign-test).

Neck dissection specimens (Table 1b)

Histopathologic examination demonstrated 35 positive specimens. Twenty-seven of these were correctly identified by palpation. Ultrasound examination and CT identified metastases in 33 and 32 specimens, respectively.
Eight positive neck dissection specimens were considered negative by palpation. Six of these were correctly assessed by ultrasound examination and 5 by CT. There were two false negative neck judgments on ultrasound. Neither of these two were correctly judged by palpation or CT. Of the 3 false negative results of CT, one was correctly identified by ultrasound examination.

Table 1b Results of palpation, ultrasound examination and CT in the assessment of cervical metastatic disease in 36 patients with squamous cell carcinoma of the upper aero-digestive tract. In this table, positive applies to necks with nodal metastases, and negative to necks without nodal involvement.

Palpation

	Metastases	No metastases
Positive	28	2
Negative	7	7
	35	9

Sensitivity of palpation: 80%

Ultrasound

	Metastases	No metastases
Positive	34	8
Negative	1	1
	35	9

Sensitivity of ultrasound: 97%

CT

	Metastases	No metastases
Positive	32	4
Negative	3	5
	35	9

Sensitivity of CT: 91%

The differences between palpation and ultrasound are statistically significant: double-sided p-value .03 (sign-test). The differences between palpation and CT, and between ultrasound and CT were not statistically significant.

Regions (Table 1c)

In 35 neck dissection specimens, 50 regions with one or more metastases (positive regions) were established. Palpation correctly assessed 30, ultrasound 45 and CT 39 positive regions. In Tables 2 and 3 the sensitivity of the diagnostic methods in the different regions of the neck is summarized. Ultrasound examination appears to be superior to CT and palpation in all regions. CT equals palpation in most regions and is slightly superior in the jugular regions only. In 4 patients with a clinically (palpatory) positive neck, ultrasound examination demonstrated metastases at a higher level in the neck in 4, and at a lower level in 3 patients. For CT these figures were 2 and 1, respectively.

Table 1c Results of palpation, ultrasound examination and CT in the assessment of cervical metastatic disease in 36 patients with squamous cell carcinoma of the upper aero-digestive tract. In this table, positive applies to regions with nodal metastases, and negative to regions without nodal involvement.

Palpation

	Metastases	No metastases
Positive	31	7
Negative	20	382
	51	389

Sensitivity of palpation: 61%

Ultrasound

	Metastases	No metastases
Positive	46	30
Negative	5	359
	51	389

Sensitivity of ultrasound: 90%

CT

	Metastases	No metastases
Positive	40	13
Negative	11	376
	51	389

Sensitivity of CT: 78%

The sensitivity-rate of ultrasound is statistically significant higher than the rate of CT (double-sided p-value .03) and palpation (double sided p-value < .001). The sensitivity-rate of CT is statistically significant higher than the rate of palpation (double-sided p-value .004) (sign-test).

Nodes (Table 1d)

Histopathologic examination of the 44 neck dissection specimens revealed a total number of 91 metastases. Palpation demonstrated 38, ultrasound examination demonstrated 66, and CT demonstrated 50 metastases. Since the number of reactive nodes were not always recorded by the pathologist, true negative rates are not available.

Table 1d Results of palpation, ultrasound examination and CT in the assessment of cervical metastatic disease in 36 patients with squamous cell carcinoma of the upper aero-digestive tract. In this table, positive applies to single metastases, and negative to nodes without metastatic involvement.
Since the number of reactive nodes was not always recorded by the pathologist, true negative rates are not available.

Palpation

	Metastases	No metastases
Positive	38	not recorded
Negative	53	not recorded
	91	

Sensitivity of palpation: 42%

Ultrasound

	Metastases	No metastases
Positive	66	not recorded
Negative	53	not recorded
	119	

Sensitivity of ultrasound: 73%

CT

	Metastases	No metastases
Positive	50	not recorded
Negative	41	not recorded
	91	

Sensitivity of CT: 55%

Table 2 The number of histologically proven metastases in each region of the neck, and the percentage detected by palpation, ultrasound examination and CT, in 36 patients with squamous cell carcinoma of the upper aero-digestive tract.

REGIONS	NUMBER	PALPATION	ULTRASOUND	CT
SUBMENTAL	0	0	0	0
SUBMANDIBULAR	3	67%	100%	67%
JUGULODIGASTRIC	35	51%[1]	69%[2]	63%[3]
MID JUGULAR	26	54%[1]	96%[2]	63%[3]
LOW CERVICAL	21	19%[1]	38%[2]	24%[3]
UPPER POSTERIOR	0	0	0	0
MID POSTERIOR	6	0	100%	0
SUPRACLAVICULAR	0	0	0	0
PRE-AURICULAR	0	0	0	0
REGIO ANTERIOR	0	0	0	0

1 $p = .03$, chi-square test
2 $p < .001$, chi-square test
3 $p = .01$, chi-square test

Table 3 The number of histopathologically positive regions, and the percentage correctly detected by palpation, ultrasound examination and CT in 36 patients with squamous cell carcinoma of the upper aero-digestive tract.

REGIONS	NUMBER	PALPATION	ULTRASOUND	CT
SUBMENTAL	0	0	0	0
SUBMANDIBULAR	3	67%	100%	67%
JUGULODIGASTRIC	20	75%[1]	95%[2]	90%[3]
MID JUGULAR	17	65%[1]	100%[2]	94%[3]
LOW CERVICAL	10	30%[1]	60%[2]	40%[3]
UPPER POSTERIOR	0	0	0	0
MID POSTERIOR	1	0	100%	0
SUPRACLAVICULAR	0	0	0	0
PRE-AURICULAR	0	0	0	0
REGIO ANTERIOR	0	0	0	0

1 $p = .05$, chi-square test
2 $p = .003$, chi-square test
3 $p = .001$, chi-square test

Multiplicity

In 16 neck dissection specimens multiple metastases were present. These were demonstrated by palpation in 5, by ultrasound in 13, and by CT in 9 neck dissection specimens. Three masses interpreted as a single node by the clinician and CT, appeared to be a conglomerate of nodes at ultrasound and histopathologic examinations. One single node at palpation and ultrasound, appeared to be a conglomerate at CT and histopathologic examination.

Discussion

In this study, the indication for a CT examination was made on clinical grounds. Therefore, the population included many patients with advanced disease and/or palpable neck masses. This selection resulted in a high incidence of nodal disease. This probably influenced the sensitivity-rates of the diagnostic methods. E.g., the sensitivity-rates of palpation for detection of patients and necks with metastatic involvement are indeed very high when compared to the sensitivity-rate in chapter II.1 (73%) and to the rates in other studies, ranging from 35-65%[1 2 3 4]. This suggests that in populations at lower risk, the sensitivity-rates must be adjusted downwards. The same bias applies to CT.
Another reason why the sensitivity-rates of CT are comparatively high, is that we included all depicted nodes, no matter what size, shape or appearance. We agree with Feinmesser et al.[5] that nodal size is not a reliable criterion to detect occult metastases as far as CT is concerned, since any size criterion will result in false positive and false negative results. As for morphoradiologic changes (central necrosis, obliteration of fascial planes, contiguous nodes) which are advocated to discern benign and malignant nodes, firstly, we agree with Feinmesser that these are relatively infrequent signs and, secondly, we support the view of Tubman[6] who states that these signs may occur in inflammatory disease as well. When these criteria would have been applied in this study, sensitivity rates of CT would have dropped.
In contrast, the sensitivity-rate of ultrasound for detection of necks with metastatic involvement does not differ from the rate which was found in chapter II.1 and measured more than 90%. (In chapter II.1, the sensitivity-rates were estimated in a population in which spectrum bias was less important).

When the results of palpation, CT and ultrasound examination are compared to each other, it appears that CT and ultrasound examination are of equal value in the detection of patients with metastatic involvement when the patients are at high risk for metastases. Both imaging techniques were characterized by higher sensitivity-rates compared to palpation. However, the differences were not statistically significant.
Multiplicity of nodal involvement and the number of nodes are best assessed at ultrasound examination, although the sensitivity of CT for the detection of single nodes may be negatively influenced by the choice for 6 mm sections: smaller sections will detect more nodes. However, smaller sections will increase the examination-time and the false positive rates.

When the regions of the neck are judged separately, the sensitivity for metastases is highest for ultrasound examination. The sensitivity for detection of single cervical lymph node metastases and the sensitivity for detection of positive regions are influenced negatively by the number of metastases missed in the jugulo-digastric and lower cervical regions. This applies for all three diagnostic methods. The reason why metastases in the jugulo-digastric region are missed, may be the complex anatomy of this region. Regarding ultrasound examination, the presence of the mandible is a limitation in handling the transducer. The number of metastases missed in the lower cervical region (including low jugular and low posterior cervical regions) is striking. In general, metastases in this region were smaller when compared to the metastases in the jugulo-digastric and mid jugular regions. This may account for the low sensitivity of the three diagnostic methods in this region. With regard to palpation, the firm and broad attachment of the sternocleidomastoid muscle to the clavicle may hinder adequate investigation in the low jugular region. The low posterior cervical region is not very accessible for clinical examination either. No explanation is found for the number of metastases ultrasound examination failed to detect in the low jugular and low posterior cervical regions. Assessment of lymph nodes in these regions, perhaps received less attention, because these regions are known to be less susceptible for metastatic disease. The low jugular and low posterior cervical regions are difficult to examine by CT because of the distribution of fat and "partial volume effect" caused by the local arrangement of musculature.

Finally, palpation failed to demonstrate a lot of metastases in the mid jugular region. This region is difficult to examine because of the localization of lymph nodes medial to the sternocleidomastoid muscle.

The values and limitations of current diagnostic methods in the evaluation of the neck in patients with squamous cell carcinoma of the upper aero-digestive tract are outlined as follows.

The next features appear to be important in a proper evaluation of cervical disease:

1 Presence or absence of node metastases, and
2 Size of the involved nodes, and
3 Multiplicity/number of involved nodes, and
4 Level/localization, and
5 Extra-capsular growth/extra-nodal tumor spread.

<u>ad 1.</u> The accuracy-rates of palpation and ultrasound examination were evaluated in chapter II.1.

For sensitivity-rates of CT we must rely on the results of other authors, since the results of the present study cannot be applied to patients at lower risk for nodal metastasis. In literature, the sensitivity-rate of CT ranges from 60%[5] to more than 90%[7 8 9 10 11].

From these data we conclude that CT and ultrasound examination are superior to palpation in screening for nodal disease.

Regarding the absence of disease, the negative predictive value of the diagnostic methods was not evaluated in the present study. Feinmesser et al.[5] calculated the

negative predictive value of palpation to be 69.2%, compared to 66.1% for CT. In chapter II.1 negative predictive values appeared to be 37.5% for palpation, and 81.3% for ultrasound examination with UGFNAB. These data indicate that ultrasound with UGFNAB may demonstrate the absence of nodal metastases more accurately than palpation and CT.
Since ultrasound examination allows reliable establishment of both the presence and the absence of metastases, we consider it to be more efficaceous than CT.
Unlike palpation and ultrasound examination, CT is a suitable modality to demonstrate retropharyngeal nodes. When nodes are suspected in this region, CT is the test of first choice.

ad 2. Measurement of the size of lymph nodes was not evaluated in this study. Although the literature on observer variation in the clinical assessment of neck nodes is sparse, the work of Warr et al.[12] supplies evidence that observer variation may be considerable. Therefore, the observations of a single examiner may not be very accurate. In contrast, current small-parts transducers are precisely calibrated and allow accurate measurement of size in all three dimensions. The same holds true for CT, but the cranio-caudal dimension in axial scanning is dependent on the thickness of the scans. Furthermore, the bulk of tumor may be overestimated on CT because of associated edema. In our experience, the size of nodes was often over-estimated by the oncologist, when compared to ultrasound examination, CT and operative findings. Therefore, we consider ultrasound examination and CT to be superior to palpation in measurement of size.

ad 3. Multiplicity of neck node metastases is an important prognostic factor in cervical disease[13 14]. In the present study, ultrasound examination appeared to demonstrate more histopathologically proven metastases than palpation and CT. Therefore, this feature is apparently best assessed by ultrasound.

ad 4. The level of lymph node metastasis is established on clinical grounds for palpation and anatomical references for ultrasound examination and CT. The accuracy of the investigative modalities in this respect was not studied, and there are few data in the literature on this issue. It is assumed that the localization of neck nodes is established with equal reliability by all methods.

ad 5. Establishment of nodal extra-capsular growth by imaging techniques was not the subject of this study. No definite data are available in the literature. In our experience, neither imaging modalities nor palpation are appropiate to assess nodal extra-capsular growth.

These data from literature, and from chapters II.1, II.2 and II.3 permit the following conclusions:

1 Ultrasound examination and CT are useful to demonstrate the presence of nodal metastasis.
2 Ultrasound with UGFNAB may exclude cervical metastasis more reliably than CT.
3 Multiple node involvement and the involvement of different neck regions is assessed more accurately by ultrasound when compared to palpation and CT.
4 Accurate measurement of nodal size requires ultrasound or CT.

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Chapter II.4

Staging of upper aero-digestive tract cancer by palpation, and ultrasound with cytologic examination

Abstract

The results of palpation, and the results of ultrasound examination of the neck supplemented with the results of cytologic examination of detected lymph nodes, were used to stage 200 patients with squamous cell carcinoma of the upper aero-digestive tract. In 134 patients the results of the diagnostic methods were in accordance with each other. In the remaining 66 patients, the findings at ultrasound examination when combined with the results of cytologic examination altered the initial staging based on palpation: 34 patients were up-staged and 32 were down-staged. Ultrasound detection of cervical lymph nodes and subsequent cytologic examination accounted for the up-staging of patients. Down-staging was by virtue of the ultrasound findings (2 patients) or the negative results of cytologic examination (30 patients). In view of the sensitivity-rate to detect lymph nodes by ultrasound examination, and the reliability of a cytological diagnosis, it is concluded that ultrasound with cytologic examination of detected nodes may influence staging of the neck in patients with upper aero-digestive tract cancer considerably.

Introduction

Cervical lymph node metastasis is one of the most ominous prognostic factors in patients with squamous cell carcinoma of the upper aero-digestive tract. The presence of a single cervical lymph node metastasis in the ipsilateral portion of the neck decreases the expected survival by 50%. A contralateral affected node also reduces the expected survival by 50%. It was demonstrated that a patient with bilateral cervical metastases has only the quarter the expected survival he or she would have if there were no nodal metastases[1].

Furthermore, the choice of treatment is greatly influenced by the demonstration of nodal disease. The evaluation of cervical nodes is therefore of paramount importance in the initial diagnostic work-up of patients with a head and neck malignancy.

In chapter II.1 and II.2 ultrasound examination and ultrasound guided fine needle aspiration biopsy (UGFNAB) of neck nodes were evaluated. It was concluded that ultrasound examination is a very sensitive technique (sensitivity 96.8%) for detection of necks with metastatic disease. UGFNAB was characterized by a high specificity (95%). The combination of ultrasound examination and UGFNAB was characterized by high positive (98%) and negative predictive values (95%) for nodal metastases, indicating that there was a high probability that nodes diagnosed as affected will indeed have metastatic disease. Conversely, a high negative predictive value indicates that cytologic examination might be useful to exclude metastases in neck nodes.

In the present study palpation of the neck is compared to ultrasound examination with cytologic examination, as far as staging of patients with squamous cell carcinoma of the upper aero-digestive tract is concerned.
In addition, the significance of negative (UG-)FNAB of palpable nodes is discussed.

Patients and methods

Between December 1984 and December 1987 two hundred patients presenting with squamous cell carcinoma of the upper aero-digestive tract were examined by palpation of the neck and ultrasound. Patients with a low incidence of cervical metastasis (T1 glottic carcinoma and carcinoma of the paranasal sinuses) were not included in this study.
Palpation was performed by a member of the oncological staff. Subsequently, RJR, RJBdJ, JSL or HvO, without knowledge of the clinical data, performed an ultrasound examination of the neck. UGFNAB was performed on nodes depicted by ultrasound examination. When more than two nodes on one side of the neck were visualized, only the most cranial and most caudal node were aspirated. When these nodes were comparatively small, the largest nodes were aspirated.
In some cases, especially in the beginning of our study, fine needle aspiration biopsy of palpable nodes was performed by the head and neck oncologist (without ultrasound guidance). In these few patients (less than 15), nodes were not examined again by UGFNAB.
Both the results of palpation and the results of ultrasound examination complemented with the results of cytologic examination, were used to stage cervical disease according UICC definitions (Appendix D).
All smears were examined by an experienced cytologist. Samples were classified according Papanicolaou. Retrospectively, Pap I and II were considered benign (negative) and Pap IV and V malignant (positive). A sample classified Pap III and smears containing neither lymphatic cells nor squamous cell carcinoma were considered as being non-diagnostic.

Results

The results are presented in Table 1. In 134 of the 200 patients the results of palpation with cytologic examination and ultrasound examination with cytologic examination were **in accordance:** 88 patients had no cervical disease, 46 had metastatic disease (19 N1, 6 N2a, 17 N2b, 4 N2c).
Thirty-four patients were **up-staged** because ultrasound examination with cytologic examination demonstrated metastases which palpation had failed to establish: 12 necks, considered not to be metastatically involved on palpation, appeared to contain metastases (10 N0→N1 and 2 N0→N2b). In 22 patients more metastases were demonstrated than estimated at palpation (7 N1→N2b, 5 N1→N2c, 4 N2a→N2b, 3 N2a→N2c, 3 N2b→N2c).
Two patients were **down-staged** due to ultrasound findings: in one case ultrasound examination demonstrated an enlarged submandibular gland, whereas the clinician had

Table 1 Staging of nodal disease in 200 patients with upper aero-digestive tract cancer.

PALPATION	ULTRASOUND+CYTOLOGY						
	N0	N1	N2a	N2b	N2c	N3	
N0	88	10	-	2	-	-	100
N1	19	19	-	7	5	-	50
N2a	1	1	6	4	3	-	15
N2b	-	2	3	17	3	-	25
N2c	3	2	1	-	4	-	10
N3	-	-	-	-	-	-	-
	111	34	10	30	15	-	200

interpreted the lesion as a suspect node (N1→N0). Another patient was down-staged because a node which was estimated to measure more than 3 cm in diameter on palpation, appeared to be less than 3 cm on ultrasound examination (N2a→N1).

Negative UGFNAB of palpable nodes

In thirty patients a palpable node appeared 'reactive' cytologically. Without (UG)FNAB these nodes would have been considered metastases (18 N1→N0, 1 N2a→N0, 2 N2b→N1, 3 N2b→N2a, 3 N2c→N0, 2 N2c→N1, 1 N2c→N2a).

Discussion

Several authors[2 3 4 5] have indicated that palpation is not a reliable method to assess lymph nodes in the neck. Therefore, imaging techniques are advocated as a necessary part of staging cervical disease. Usually CT, MRI, and ultrasound examination are recommended. Although these techniques may be superior to palpation in the detection of lymph nodes in the neck, they do not discriminate between reactive nodes and metastases. This is basically due to the lack of specificity of the images obtained. Cytologic examination may provide additional information.

According to Linsk and Franzen[6], enlargement of a node by metastatic deposits indicates fairly diffuse involvement or replacement by tumor. As a result, random aspiration of an enlarged metastatic node will almost invariably obtain tumor cells. Aspiration of a clinically enlarged node that fails to produce tumor cells is fairly good evidence against metastasis and should lead to the consideration of inflammation or lymphoma. These statements are confirmed by other authors, who concluded that cytologic examination of palpable nodes is an accurate method for differentiation between benign and malignant disease[7 8 9 10 11 12].

The high sensitivity of ultrasound examination for the detection of cervical nodes, and the previously demonstrated test-characteristics of FNAB and (UG-)FNAB (chapter II.2), actuated the present study in which ultrasound examination with cytologic examination was applied for staging patients with squamous cell carcinoma of the upper aero-digestive tract.

Up-staging: detection of non-palpable metastases

As stated above, cytologic examination is a reliable method to demonstrate cervical metastatic disease. This holds true for material obtained in a conventional way, as well as by UGFNAB.
Therefore, the up-staging of 17% of our patients seems justified on the basis of positive findings on UGFNAB.

Down-staging: exact measurement of size

The size of neck nodes is also an important factor in staging cervical disease. The size may be estimated incorrectly at clinical examination[13 14]. The current small-parts transducers are precisely calibrated and allow accurate measurement of size in all three dimensions. In our study, 1 patient was down-staged because ultrasound examination depicted a node with smaller dimensions than was judged by palpation (1 N2a→N1).

Down-staging: differentiation from other masses in the neck

It may be difficult to discern lymph nodes and other masses in the neck at clinical examination: occasionally, a prominent carotid bulb is misinterpreted as a lymph node, particularly if the bulb wall has undergone atherosclerotic calcification that reduces elasticity. It may be clinically difficult to differentiate regional structures from nodes in the submandibular triangle. Occasionally the submandibular glands show variation in contour and texture due to inflammatory disease, sialo-adenose, or obstruction of the gland. These firm areas may be incorrectly identified as fixed nodes. The jugulo-digastric region may also erroneously be considered to have metastatic disease. A hypertrophic masseteric muscle, the parotid gland, the mandible, the digastric and sternocleidomastoid muscles, vascular structures and the transverse process of C1, may cause interpretive confusion. Ultrasound examination however, can differentiate cervical nodes from other cervical lesions, as will be demonstrated in Part III.
In this study, one patient with squamous cell carcinoma of the floor of the mouth and a suspect lump in the neck was down-staged, because ultrasound examination demonstrated that the mass was actually an enlarged submandibular gland. It was clear from ultrasound findings that the enlargement was due to obstruction of Stensen's duct by neoplastic invasion (1N2a→N0).

Down-staging: negative cytologic diagnosis

In contrast to the acknowledged value of a positive cytologic diagnosis, the significance of a negative cytologic result is often doubted. As a consequence, palpable nodes which are clinically suspect, are often, despite negative cytology, considered to be lymph node metastases.

However, it was demonstrated in chapter II.2 that the probability that nodes with negative cytology indeed are benign, is high. Earlier reports mentioned similar properties of cytologic examination to exclude metastasis in palpable cervical nodes (sensitivity ranging from 92 to 99%) [67 10]. In other words: a negative (UG-)FNAB is as reliable as a positive one. Therefore, down-staging of patients with palpable nodes and negative (UG-)FNAB, seems justified too. It is interesting to notice that the proportion of patients down-staged by virtue of the results of cytologic examination (15%), is almost similar to the false positive rate of palpation which is given in relevant literature (chapter II.1). In our opinion, this gives further support to the consideration of down-staging on the basis of the results of cytologic examination.

In summary

In 66 of 200 patients (33%) presenting with squamous cell carcinoma of the upper aero-digestive tract, ultrasound examination with (UG-)FNAB changed the initial staging of these patients which was based on palpation findings: up-staging by ultrasound detection and subsequent UGFNAB; down-staging by correct assessment of size of nodes; down-staging by identifying other cervical lesions which were erroneously interpreted as being nodes by the clinician and down-staging based on negative cytologic diagnosis of (UG-)FNAB.
On grounds of these results, we consider ultrasound and UGFNAB an accurate method for staging of the neck in patients with upper aero-digestive tract cancer.

The aims of ultrasound with UGFNAB-staging in patients with clinically positive necks might be:

1 To determine and quantify the involvement of neck nodes. Ultrasound allows precise measurement of size. It may also show whether multiple or solitary nodes account for the abnormalities on palpation. This might help to separate the N2b category from the other categories and to distinguish more accurately between N1 and N2a necks.

2 To differentiate nodes from other masses in the neck. This might reduce the false positive rate of palpation.

3 To detect contralateral spread. This can up-stage a neck to N2c.

4 UGFNAB might help to differentiate reactive nodes from true metastases, which might down-stage necks.

In patients with clinically negative necks ultrasound with UGFNAB may serve one of the two following purposes:

1 To detect nodes which are not felt at clinical exam.
2 To confirm the clinical impression of a negative neck.

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Chapter II.5

Comment

No primary tumor in the head and neck can be treated without concomitant attention directed to regional metastases, and there are many questions pertaining to the correct management of this aspect of disease. One of these is the assessment of cervical metastatic disease. The importance of ascertaining the presence or absence of neck node involvement is attended by a large volume of data in literature which relate prognosis to the extent and distribution of metastatic nodes. A discussion on this specific topic is beyond the scope of this study, and we confine ourselves to the statement that the assessment of cervical disease is of paramount importance in the management of patients with upper aero-digestive tract cancer.
In order to allow comparison of the properties of ultrasound with UGFNAB, the pros and cons of the current diagnostic methods are summarized as follows.

Palpation

Evaluation of the neck has always been by physical examination. Since the fingers are not terribly sensitive probes for small nodes containing tumor, a substantial false negative rate may be anticipated. Since also many of the primary tumors are sites of local infection, the presence of reactive lymphoid hyperplasia might result in a number of false positive evaluations as well. Moreover, as stated in chapter II.4, interpretive confusion may be caused by the carotid bulb, the contents of the submandibular triangle and the structures in and near the jugulo-digastric region. These structures may be incorrectly identified as lymph nodes clinically. These statements from the literature concerning palpation are confirmed by our own results, as described in chapter II.1, II.3 and II.4. These results were obtained by experienced head and neck oncologists, and it can be expected that palpation is even less reliable in less experienced hands.

Another drawback of palpation is the lack of objectivity: the thickness of the patient's skin, the amount of subcutaneous fat, and the width and mass of the sternocleidomastoid muscle are all variables that could potentially lead to a lack of agreement if measurements are taken by multiple individuals.
According to Keane[1], studies of observer variation have received little attention in discussions regarding clinical staging. There is evidence that observer variation is a significant source of error in the measurement of size of malignant neck nodes. This question was studied by Warr et al.[2]. The findings from their study demonstrated clearly that even with scrupulous examination by skilled observers, a significant degree of error existed in estimating size. These statements are confirmed by the observations in clinical practice by Snow[3].

On the basis of the above stated, it is concluded that palpation is characterized by considerable false positive and false negative rates, and by a considerable observer variation.

Since the physical examination is obviously imperfect, investigators have been exploring various imaging techniques, such as lymphangiography, CT, MRI, and ultrasound.

Lymphangiography

Before the advent of CT, the only pertinent radiographic examination was cervical lymphangiography. This procedure was associated with a high frequency of technical failure, primarily due to deep-lying, extremely small lymphatics in the area most commonly used for injection of contrast material: the retro-auricular region. In addition, these studies were fraught with interpretive difficulties, primarily related to the inability to distinguish malignant nodal from reactive nodal filling defects. Proximal metastatic nodal disease near the injection site could prevent visualization of distal lymph nodes. Finally, previous surgery, disease, or irradiation could alter or disrupt the usual lymphatic pathways, leading to either a nondiagnostic or a misleading lymphangiogram[4 5].

CT

The most promising techniques appeared to be CT and MRI. Several studies have indicated that CT may provide important information on the true status of the cervical lymph nodes[6 7 8 9 10 11]. These authors stated that CT has a greater sensitivity and greater specificity than physical examination in predicting cervical metastases. However, much like physical examination of the neck, CT evaluation of the cervical lymph nodes is hindered by the multiple anatomic structures in this region. Even with excellent technique and high levels of contrast for visualization of the blood vessels, lymph nodes can be confused with, or obscured by these structures. If contrast medium cannot be given, or if the patient is thin and without fat planes, proper assessment of the neck is further compromised. These statements are supported by the work of Feinmesser et al.[12], who concluded in a clinical, radiographic, and pathologic-correlative study, that CT offers little advantage over physical examination in the detection of metastatic neck disease. In that study, 5 to 10 mm axial sections were used, and it is probable that smaller sections and more sophisticated equipment may yield higher sensitivity-rates. However, increasing sensitivity-rates lead to an increase of false positive results, since the problem of the lack of specificity of the CT images remains unsolved.
Criteria which have been developed for differentiation between reactive nodes and metastases are not satisfactory. The size criterion is quite arbitrary: the lower the limit used as a cut off between normal and malignant nodes, the higher the false positive rates. Therefore, we agree with Close[10] that the size of lymph nodes on CT alone has not proved to be a reliable indicator of malignancy.

Radiological criteria include the depiction of central necrosis (a central area of low attenuation with a surrounding irregular wall). Although this sign is fairly characteristic, fatty nodal replacement may resemble central necrosis and this can occur in postinflammatory and postirradiation nodes[13].

As for other radiological changes (obliteration of fascial planes, contiguous nodes), firstly, we agree with Feinmesser[12] that these are relatively infrequent signs and, secondly, we support the view of Tubman[14] who states that these signs may occur in inflammatory disease as well.

It has also been suggested that spherical nodes are more likely to contain metastatic disease than are flat or ovoid nodes[13]. However, CT is two-dimensional and the interpretation of the shape of a three-dimensional structure such as a lymph node require contiguous, thin sections. This would increase examination-time, costs and radiation-exposure for a sign which is not a very reliable indicator of malignancy[10].

Finally, it must be borne in mind that there is a considerable proportion of metastases which are small and lack radiological changes, and would be considered reactive on CT. Most authors fail to address this important group of false negative results.

To conclude, we agree with Snow[3] that CT may play a role in the retropharyngeal regions, and in short, fat, or muscular necks. Differentiation between reactive nodes and metastases on the basis of size or morphoradiologic criteria seems impossible.

MRI

Although there is little statistically relevant correlation between pathologic and MRI findings at this time, it seems that this technique holds a promise for the future[11]. There is initial evidence to suggest that areas of high T2 signal intensity within a lymph node may correspond to sites of tumor necrosis, and that MRI imaging may become a sensitive technique for the evaluation of these metastatic nodes.

Ultrasound

Several authors have addressed the subject of ultrasound in metastatic neck disease in patients with upper aero-digestive tract cancer. Early reports were focused on the ability of ultrasound to quantify lymph node size and volume, and the possibilities to define the relationship of palpable nodes to adjacent structures [15,16,17]. In 1984, Bruneton[18] was the first to recognize the value of ultrasound to detect subclinical disease. He reported sensitivity to be 92.6% and specificity as high as the unparalleled figure of 91%. It may also be noted that in the same study the specificity of clinical examination was exceptionally high too: 97%.

Like Hajek et al[19] and Eichhorn et al[20], we are convinced that benign and malignant lymph node enlargement <u>cannot</u> be differentiated on grounds of ultrasound characteristics only. There is however a major discrepancy in diagnostic approach between these and our studies. In our opinion, the impossibility to discriminate between benign and malignant nodes leads to an unacceptably large proportion of false positive results, which may result in up-staging and over-treatment (chapters II.1, II.3, II.4). Therefore, we consider the employment of cytologic examination to be essential: the values of ultrasound and cytologic examinations were demonstrated to be complementary and the combination of these two investigative methods added greatly to the significance of the procedure.

Cytopathology

The aspirates of cervical lymph node metastases are often rich in tumor cells and these cells often dominate the smear. The cytologic presentation depends on keratin formation and the degree of keratin formation by the tumor. Keratinizing cancers are readily identified when cells with abundant, sharply demarcated, keratinized cytoplasma and polymorphic nuclei are present in smears. This pattern accounts for the majority of aspirates from squamous cell carcinoma metastases. The identification of non-keratin-forming cancers may be more difficult. These may show anaplastic cells with marked variation in size and shape.

Difficulties may arise in aspirates from branchiogenic cysts, carotid body tumors, and tumors of the dermis (e.g. the calcifying epithelioma of Malherbe). These disorders may yield well differentiated squamous cells showing keratinization, resembling well differentiated carcinoma. Cholesterol crystals in branchiogenic cysts, areas of calcification and foreign body giant cell reactions in the calcifying epithelioma of Malherbe, and pale cells with abundant cytoplasma and vesicular nuclei in carotid body tumors may give a clue to the diagnosis.

Another pitfall is the smear showing necrosis only. Such smears may be both from inflammatory and neoplastic disorders. These smears should be scrutinized for interpretable cells. When these are not present, the aspiration should be repeated. Metastases from poorly differentiated carcinoma may resemble lymphoma. Immunocytologic techniques which are currently available may supply data for correct interpretation.

Finally, a non-diagnostic cytologic diagnosis should be interpreted as having provided no clinical information and non-diagnostic is not synonymous with negative. Clinical judgment must decide whether to repeat the aspiration, to treat, or to follow up the patient.

To prevent a wrong cytopathological diagnosis, the cytopathologist should be supplied with extensive clinical information: sex and age of the patient, clinical signs and symptoms, the site of the aspiration, laboratory data, imaging findings, site and classification of the primary tumor when available, etc. When doubt persists, our cytopathologists prefer to mention a differential diagnosis, rather than the most likely diagnosis.

As discussed in chapter II.4, random aspiration of an enlarged metastatic node will almost invariably obtain tumor cells. When no tumor cells are found in an enlarged node, this is fairly good evidence against metastasis. In chapter II.2 it was demonstrated that when UGFNAB is used, this applies for non-palpable lesions as well. When a node is not enlarged, it is not picked up by the clinician, nor by the sonographer. Since these nodes cannot be aspirated, microscopic tumor deposits in these nodes, will not be recognized. Microscopic nodal involvement may be recognized in an enlarged node, when the node is sampled in different areas. In our opinion, this is best accomplished with aspiration under ultrasound guidance.

In conclusion, the assembled information obtained by the physician and an experienced cytopathologist can provide an accurate assessment of the cervical lymph nodes in patients with upper aero-digestive tract cancer.

Ultrasound with UGFNAB

The concept of methodical use of both cytologic examination and an imaging technique in the evaluation of patients with squamous cell carcinoma of the upper aero-digestive tract is new. The results of this diagnostic procedure are very promising (part II): neither clinical examination, nor modern imaging techniques other than ultrasound are characterized by high sensitivity and high specificity. High sensitivity of a diagnostic test implies that the test may be used to exclude a strongly suspected diagnosis or to confirm that a disease is not present when the clinician must be virtually certain. High specificity is needed to verify the presence of a disease for which there is little clinical evidence or when the clinician must be virtually certain of a diagnosis[21]. In other words: a test with high sensitivity and high specificity is suitable for detection, demonstration and exclusion of disease.

The validity of a diagnostic test is also determined by the absence of bias, the absence of observer variation, and the precision of the test. Many types of bias can influence the test parameters, such as spectrum bias, test-review bias, diagnosis-review bias, and uninterpretability bias[22].
Spectrum bias may occur when the patient sample does not include an appropriate spectrum of mild and severe, treated and untreated disease, plus individuals with different but commonly confused disorders. This type of bias may have influenced our results: the study populations in chapter II.1, II.2, and II.3, contained patients undergoing neck dissection. Since in our department elective neck treatment was with radiation therapy rather than surgery, the population contained relatively few patients with negative necks. This applies especially to the patients in chapter II.3, in whom a pre-operative CT was a condition to enter the study. Since the indication for CT was made on clinical grounds (advanced primary disease, masses in the neck), prevalence of nodal disease was very high. For all studies, the spectrum bias may have caused an over-estimation of the sensitivity-rates. Another cause for over-estimation of the sensitivity-rates may have been the fact that palpation and ultrasound with UGFNAB were used to select patients for neck dissection: when the results of these tests were negative, the patient was less likely to be referred to the gold standard procedure

than if the tests were positive (verification bias). This also increased the false positive rate: as most patients with a positive test result were referred for the gold standard procedure, there was a disproportionately large number of false positive results. On the basis of the above stated, the sensitivity rate and the false positive rate should be adjusted downwards.
Bias may also occur when the diagnostic tests and the gold standard were not applied in blind fashion (test-review bias and diagnosis-review bias). Whereas the results of palpation occasionally may have been influenced by the results of CT, care was taken to avoid that ultrasound examination was not performed blindly. The cytopathologic and histopathologic examinations were performed with knowledge of the histological type of the tumor (when available) only. On these grounds it is assumed that these types of bias were of minor importance in these studies.
Uninterpretability bias may arise when not all subjects or specimens provide interpretable test results. Since ultrasound examination and cytologic examination can be performed in almost any patient, the intrinsic uninterpretability bias is small. Uninterpretability may occur in patients with a beard or with a tracheostomy. These conditions are random with respect to disease, and they will not affect the estimated test parameters. As for cytologic examination, the number of uninterpretable results is listed separately in chapter II.2. Concerning UGFNAB, the number of uninterpretable results is low, and does not influence the test characteristics.
How much to adjust the test characteristics in view of the bias which may have occurred, is a current area of research[22,23]. Our data did not allow to apply these new techniques from the field of decision analysis to our results.

Since both ultrasound and cytologic examination require properties such as skill and experience, one might anticipate a considerable observer variability. Although this issue was not the subject of our study, we have the impression that observer variation is less than could be expected. This is based on our experience that the ultrasound technique and the reading of the images are readily transferable to interested radiologists. Regarding cytologic examination, in a recent study on interobserver variability in the interpretation of fine needle aspiration biopsy of head and neck masses, it appeared that variability was low for squamous cell carcinoma[24]. Whether the interobserver variability influences the validity of ultrasound with cytologic examination as a diagnostic test, will be subject of further studies.

Possible impact of ultrasound with UGFNAB on clinical management

On the basis of the test-characteristics of ultrasound with UGFNAB, it is tempting to philosophize on the possible impact of use of this diagnostic procedure on clinical management.
It is important to separate our results into two categories. Demonstrating metastases by ultrasound examination and confirming these by cytologic examination is the most important

outcome of this study, and will be the least under discussion, since the value of a positive cytologic diagnosis is well recognized. The second category is made up by the negative results of the procedure. The significance of these results will be debatable, since it will be put forward that ultrasound examination cannot depict microscopic deposits of carcinoma in lymph nodes, and the value of a negative cytologic diagnosis is not recognized and in fact often doubted.
Therefore it is stated, that the relevance of a negative result of ultrasound with UGFNAB will become clear, only when other investigators will confirm our results and after careful follow-up has proven that patients with a negative result of the procedure, are at lower risk for a recurrence in the neck.
The possible impact of ultrasound with UGFNAB on clinical management will be discussed in the following sections:

II.5.1 Possible effects of positive results of ultrasound with UGFNAB in the management of the clinically negative neck
II.5.2 Possible effects of positive results of ultrasound with UGFNAB in the management of the clinically positive neck
II.5.3 Possible effects of negative results of ultrasound with UGFNAB in the management of the clinically negative neck
II.5.4 Possible effects of negative results of ultrasound with UGFNAB in the management of the clinically positive neck

II.5.1 Possible effects of positive results of ultrasound with UGFNAB in the management of the clinically negative neck

The most important effect of ultrasound with UGFNAB is the up-staging of a selection of patients with upper aero-digestive tract cancer. The patients with clinically occult (ipsi- and/or contralateral) neck disease as identified by the procedure may be treated more adequately:
- patients who would not have received any neck treatment on grounds of the assumed low incidence of occult metastases, would benefit through getting treatment for the neck;
- patients who would have been treated by elective radiation therapy would receive a therapeutic dose of 70 Gy, instead of 50 Gy. This might reduce neck relapse and improve survival of these patients;
- assuming that radical neck dissection is to be preferred in metastatic neck disease, patients who would have been subjected to elective modified neck dissection, would benefit through undergoing therapeutic radical neck dissection.

Another group of patients in which treatment-planning may be influenced by the results of ultrasound with UGFNAB are the candidates for major surgery or other types of farreaching therapy for the primary tumor. The establishment of e.g. bilateral, multiple metastases by ultrasound with UGFNAB may be reason to refrain from these kinds of therapy in selected cases, on grounds of poorer prognosis than was previously expected. Currently, in our hospital, the patients with esophageal cancer are not operated upon anymore when ultrasound with UGFNAB demonstrate metastatic node involvement[25]. Instead, these patients are now receiving palliative radiotherapy.

II.5.2 Possible effects of positive results of ultrasound with UGFNAB in the management of the clinically positive neck

As stated in chapter II.4, a positive result of ultrasound with UGFNAB in these patients may result in:

- exact quantification of the involvement of neck nodes: ultrasound allows precise measurement of nodal size and may show whether multiple or solitary nodes account for the abnormalities on palpation. This might help to separate the N2b category from the other categories and to distinguish more accurately between N1 and N2a necks;
- detection of contralateral spread, which may upstage a neck to N2c.

II.5.3 Possible effects of negative results of ultrasound with UGFNAB in the management of the clinically negative neck

One of the basic issues in the management of patients with upper aero-digestive tract cancer, the issue of elective treatment of the neck, is still not settled[26 27 28 29]. The controversy is very complicated and discussion of the pros and cons is far beyond the scope of this study. The problem is sketched by the following: high incidence of occult metastases (up to 70% for naso-, oro- and hypopharyngeal cancer, Appendix E), the effectiveness of elective neck treatment (cure-rate more than 90% for both radiation therapy and surgery) and the failure of current diagnostic tests to detect the earliest conversion, are in favour of elective neck treatment. Opponents put forward that there has been no study demonstrating higher cure-rates for patients who underwent elective neck treatment compared to patients subjected to the wait and see policy. Morbidity and mortality, and failure-rates of elective neck treatment (less than 10% with primary tumor control; considerably more with uncontrolled primaries) are some other arguments against elective neck treatment.

Theoretically, improved diagnostic acumen could influence two aspects of this complicated matter:

1 the number of false negative results in the evaluation of patients with a clinically negative neck;

2 early detection of conversion.

The most important outcome of improved diagnostic acumen will be a considerable decrease in the number of patients amenable to elective treatment: a large proportion of patients with occult disease clinically, will be identified as having metastatic neck disease by ultrasound and UGFNAB. These patients, as discussed in section II.5.1, will be subjected to therapeutic treatment instead of undergoing elective treatment. The remaining patients, with a negative neck on palpation and ultrasound with UGFNAB, will be at lower risk for occult metastases. The new diagnostic information supplied by a negative result of ultrasound examination with UGFNAB may change (decrease) the uncertainty about the true status of the patient's cervical nodes. Bayes' theorem can be used to estimate how much the uncertainty has decreased. Bayes' theorem is used in medical decision analysis to interpret the new diagnostic information supplied by a diagnostic test[23].

To use Bayes' theorem one must estimate the probability of disease before the new information was gathered (prior probability) and know the sensitivity and specificity of the test. The probability of disease that results from interpreting new diagnostic information using Bayes' theorem is called the posterior probability.

When estimating the effect of a negative result of ultrasound examination with UGFNAB in a clinically negative neck, a derivation of Bayes' theorem may be used: pp = p x (1-sensitivity) / p x (1-sensitivity) + (1-p) x specificity. In this equation p is the prior probability and pp is the posterior probability. For a given primary tumor, the incidence of occult metastases in a clinically negative neck is known from literature (Appendix E), and can be used as an estimate of the prior probability. The sensitivity and specificity of ultrasound with UGFNAB were demonstrated to be .96 and .93, respectively (chapter II.1). However, our results may be positively influenced by our special efforts within the scope of this study and the high incidence of occult metastases in the patients studied. In addition, ultrasound examination with UGFNAB may be less sensitive in detecting a disease in an early stage than it is in an advanced stage. These aspects were discussed in a previous section. Therefore, an estimation of sensitivity and specificity for all patients with upper aero-digestive tract cancer may be between .75 and .9 (compared to a sensitivity-rate of .96 and a specificity-rate of .93 in our study).

The above mentioned variables are presented in fig. 1:

- the prior probability (p) of occult metastases, which is defined as the incidence of occult metastases, is known from the literature. Depending on location, size and T-stage of the primary tumor p will be between zero and .7;
- the accuracy of ultrasound with UGFNAB may vary between .75 and .9 and is represented by the curves in the diagram;
- the incidence of occult metastases, given a clinically negative neck and a negative result of ultrasound with UGFNAB, is the posterior probability (pp).

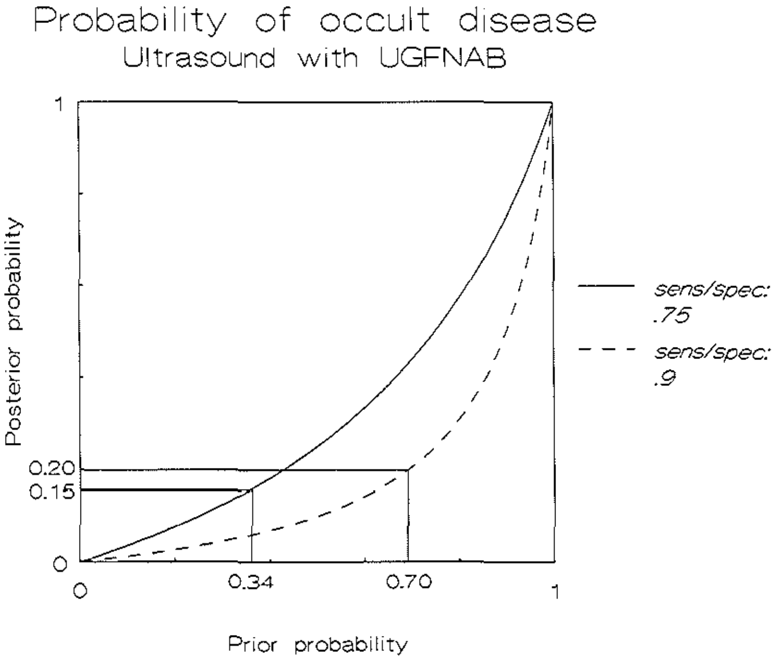

Fig. 1 Diagram showing prior and posterior probability of occult neck disease when ultrasound with UGFNAB is performed in patients with clinically negative necks.

Two examples may elucidate the meaning of fig. 1:

1 with an accuracy of only .75, the posterior probability of occult metastases for e.g. T1,2 supraglottic cancer would be about .15, instead of .34 (the prior probability of occult metastases);

2 when ultrasound with UGFNAB would be as accurate as demonstrated in part II of this study, e.g. an accuracy-rate of .9, the incidence of occult metastases in a neck negative on ultrasound with UGFNAB in a patient with oropharyngeal cancer would be lower than .20, compared to .70 in a neck negative on palpation only.

The consequences for clinical management are also determined by the incidence of occult metastases which is considered to be an indication for elective neck treatment: this may vary between institutions and ranges from .05 to .30[11 27 29 30].
(fig. 2 and 3). The calculations in fig. 2 and 3 depart from the assumption that the indications for elective neck treatment remain the same when ultrasound examination and UGFNAB are employed.

For institutions where an incidence of occult metastases of .05 is already considered an indication for elective treatment (fig. 2) and the sensitivity/specificity of ultrasound examination would appear to be only .75, the necessity for elective neck treatment in

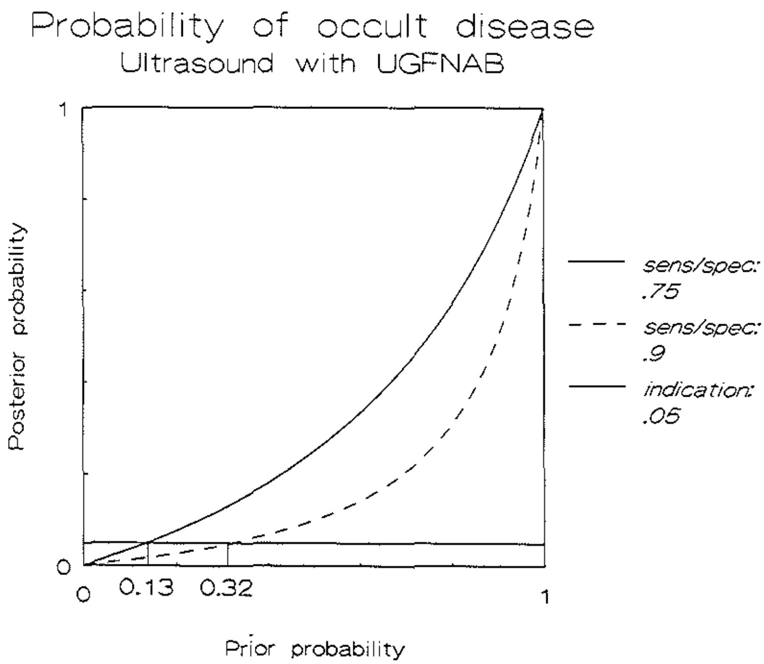

Fig. 2 *Diagram as fig. 1. The incidence of occult metastasis which is considered an indication for elective neck treatment is .05.*

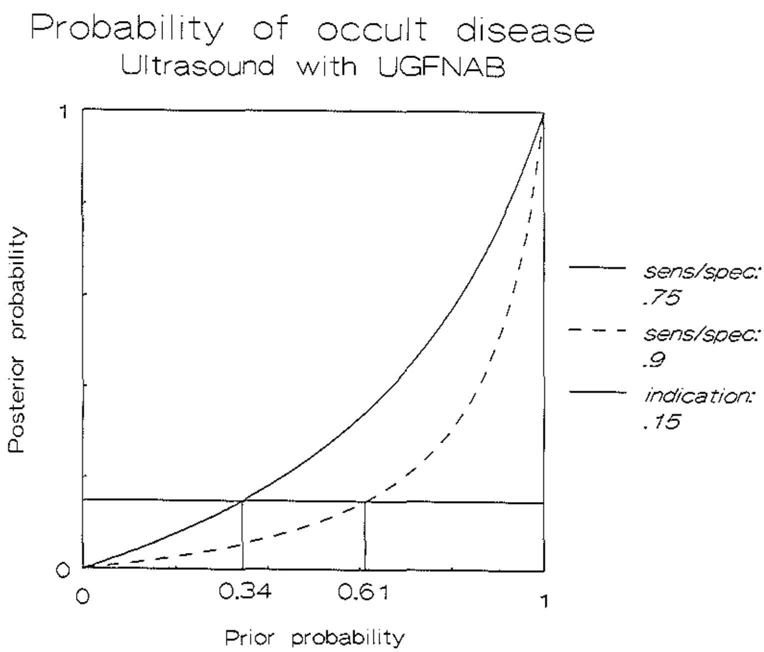

Fig. 3 *Diagram as fig. 2. The incidence of occult metastasis which is considered an indication for elective neck treatment is .15.*

patients with an incidence of occult metastases lower than .13 (e.g. early glottic, T1 oral and all T-stages of sino-nasal cancer) would be open to discussion. When sensitivity/specificity would appear to be .9, this would also include patients with less than 32% incidence of occult metastases (e.g. T1,2 supraglottic, T1,2 soft palate and T3,4 glottic cancer).
A more widely accepted indication for elective treatment is an incidence of .15 (fig. 3). The possible consequences of a negative ultrasound examination with UGFNAB would be much greater with this indication: with a sensitivity/specificity of only .75, elective neck treatment will be disputable for patients with a prior probability of less than 34% (e.g. T1,2 glottic, T1 oral, all T-stages of sino-nasal, T1,2 supraglottic, T1,2 soft palate and T3,4 glottic cancer). With sensitivity/specificity-rates of .9, elective neck treatment in patients with higher incidence of occult metastases (up to 61%) would be open to discussion too. In cancer of the naso-, oro- and hypopharynx elective treatment will still be beyond discussion.

From these examples it is clear that a more accurate assessment of the clinically negative neck may influence the concept of elective neck treatment: a selection of patients with clinically negative necks and negative on ultrasound with UGFNAB, might be considered for a wait and see policy for the neck, instead of undergoing elective neck treatment.
There will remain a proportion of patients in which ultrasound with UGFNAB fails to demonstrate metastatic neck disease: microscopic disease in nodes that are not enlarged, will continue to evade recognition. Although the biological behaviour of microscopic deposits of carcinoma in patients with controlled primaries is not precisely known, it is probable that these patients subjected to a wait and see policy, will show conversion during follow-up. In these patients, ultrasound examination would allow the earliest detection when performed frequently. Assuming that early detection of conversion is beneficial, early detection may improve the poor survival-rates (50%)[29,30] of secondary neck treatment and might increase over-all survival-rates of patients not electively treated. As at present survival-rates of the wait and see policy and elective treatment do not differ significantly, early detection may favour the wait and see policy too. This implies that patients should be considered for a wait and see policy under the express condition of regular follow-up by ultrasound with UGFNAB only.

The status of cervical lymph nodes is of paramount importance: when nodal metastases are present on admission or develop during follow-up, survival roughly decreases by half[31]. Strategies in management of the neck, which have proven to be quite satisfactory, must therefore not be changed overnight. Nevertheless, in our opinion a negative result of ultrasound with UGFNAB may reduce some of the uncertainty which exists on the true status of cervical nodes. As the concept of elective neck treatment is based on this uncertainty, recognition and confirmation of the significance of this new diagnostic procedure, may indeed influence the management of patients with clinically negative necks in future.

II.5.4 Possible effects of negative results of ultrasound with UGFNAB in the management of the clinically positive neck

Negative results of UGFNAB

At present, palpable cervical nodes are considered to be metastases on grounds of dimensions, character, site and T-stage of the primary tumor. Affirmative value is attached to a positive cytologic diagnosis; a negative cytologic diagnosis is considered to be of much less value by many clinicians. We believe however, that a negative result of cytologic examination is almost as reliable as a positive one. This statement is based on high sensitivity, specificity and negative predictive value of UGFNAB in our study, and high accuracy of cytologic examination in other studies[32 33 34]. It is on grounds of the above mentioned studies and the results in chapter II.2, that it seems justified to consider palpable nodes benign when the cytologic diagnosis is negative. As outlined in chapter II.4, this may lead to down-staging of a considerable proportion of the patients.

An entirely different aspect of the presence of benign cervical nodes in patients with upper aero-digestive tract cancer, is their significance in the immunological response of the patient to the tumor. Until now, few studies have dealt with this issue. Careful study of survival-rates in some studies however[35 36 37], reveals higher survival of patients with histologically negative necks (classified clinically as having neck disease) compared to patients without palpable nodes and histologically negative necks:
Mendelson[35] reported on the value of neck dissection in the treatment of carcinoma of the anterior two-thirds of the tongue. In this study, the 5-year survival-rate of patients with clinically N1 necks, but histologically negative neck dissection specimens, was 87%, compared to 79% for N0 necks which were histologically negative.
Similarly, Shah[36] reported higher 5-year survival for patients with false positive necks: 94% compared to 81% for true negative necks; these patients were patients with supraglottic cancer.
Finally, Spiro[37] studied cervical node metastasis in patients with oral cavity and oropharyngeal cancer. When there was no palpable cervical adenopathy and the result of histopathologic examination of the neck dissection specimen was negative, 5-year survival was 59%. For patients with clinically positive nodes which were histologically negative, the survival-rate was 63% for solitary palpable nodes, and even 67% for multiple nodes.
Although these studies were retrospective studies which were not focused on this specific topic, and the differences were not very impressive, the observation that enlarged, benign nodes may reflect an adequate and beneficial reaction on the primary tumor, requires further study in our opinion. Support for this view may be found in the study of Berlinger[38], who studied sections of lymph nodes draining head and neck squamous carcinoma and found significantly improved survival in patients whose regional lymph nodes showed hyperplasia:

expanded inner cortices or increased numbers of germinal centers, denoting active immunological response.
Assuming that benign lymph node enlargement reflects a more adequate immunological response, examination by UGFNAB may discriminate between two groups of malignant lesions which may appear to differ in biological behaviour.

Negative results of ultrasound examination

Finally, ultrasound examination allows differentiation of true nodes from other masses in the neck. This may reduce the false positive results of palpation caused by the caudate pole of the parotid gland, enlarged submandibular glands, or other benign masses in the neck. Sometimes, interpretive confusion of palpation is caused by extension of a primary oro-pharyngeal or laryngeal tumor in the neck. Although there are no published data on this latter subject, it is our experience that these tumors may be recognized by ultrasound as well.

Ultrasound with UFGNAB may influence some other issues in clinical management of cervical metastatic disease. These will be discussed subsequently.

Modified neck dissection

Since the 1970s the use of various types of modified neck dissection (MND) has increased greatly. Mostly, MND is performed exclusively in the elective treatment of patients with upper aero-digestive tract cancer. Byers et al.[39] demonstrated how variations of the MND can be selected based on site and extent of the primary. MND has been advocated for N1-neck disease as well. Ultrasound/UGFNAB may influence the concept of MND in several ways:

- when there is an indication for elective neck treatment, ultrasound and UGFNAB may be used for confirmation of a clinically negative neck, thereby supporting the choice for MND instead of RND;
- when MND is used for management of N1-necks as well, ultrasound/UGFNAB may be used to exclude metastases in other regions of the neck confirming the choice for MND;
- in necks with metastatic neck disease, the demonstration of multiple nodes in different regions may change the choice for MND into RND.

Follow-up

Ultrasound examination may be of value in assessing postirradiation or postsurgical necks which may be very difficult to palpate accurately. Evaluation of areas of induration or vague masses can alleviate the clinical worry that these may be residual or recurrent disease. In case of doubt, or when a mass is demonstrated, UGFNAB may supply further information.

Besides, ultrasound may be useful to follow-up patients who are treated by radio- and/or chemo-therapy. Measurement of nodal size on the basis of ultrasound findings may allow evaluation of the effect of therapy.
However, cytologic examination of nodes which are irradiated previously may yield a false positive result (chapter II.2).

Carotid artery invasion

Accurate preoperative assessment of malignant invasion of the carotid artery is important when planning surgery. In fact, resectability of cervical metastases is determined to a great extent by carotid artery invasion. Carotid artery invasion however is very difficult to establish: CT is not accurate in assessment of carotid artery invasion[40 41]; angiography may demonstrate advanced invasion but cannot rule out subtle changes, and the value of MRI remains to be studied[41].
Recent reports on the value of ultrasound in the preoperative assessment of the carotid artery claim excellent results and negative predictive value is reported to be very high[40 41 42]. These studies however, are not very convincing. The low number of patients included in these studies may explain the low number of false negative results, because carotid artery invasion is a relatively infrequent occurring phenomenon. In addition, true positive findings were not subtle and there was a considerable number of false positive results caused by prior surgery or irradiation.
In our experience, ultrasound examination may exclude carotid artery invasion by the depiction of fascial planes between the metastatic node and the artery. Furthermore, ultrasound examination may depict gross invasion. In the majority of patients with clinical suspicion of invasion however, ultrasound shows merely compression, not allowing a reliable judgment on invasion.
Color-Doppler flow imaging may depict very subtle flow changes caused by wall disturbances. This technique however does not allow differentiation between athero-sclerosis and malignant invasion in our experience.

Other epithelial and non-epithelial malignancies in the head and neck

Ultrasound may be used for detection of lymph node metastases in other head and neck malignancies since lymph node enlargement of any cause may be depicted by ultrasound[5]. Sensitivity-rates may differ because of different ultrasound characteristics of different tumor-types. The accuracy of UGFNAB in these other histological types should be studied for judgment of the specificity of the combined procedure (ultrasound examination with UGFNAB).

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PART III

Evaluation of head and neck masses

Introduction

The evaluation of neck tumors is a diverse and extensive topic. Congenital and inflammatory masses, and benign and malignant neoplasms may present as a neck tumor (Table 1). In addition, there are several diagnostic procedures and approaches that have recently been developed to aid the clinician in the diagnostic process. Therefore, the potential for confusion is substantial, and it is apparent that a systematic approach to the evaluation of a neck mass is essential.

Table 1 Differential diagnosis of a lump in the neck.

Congenital lesions
- thyroglossal duct anomalies
- laryngocele
- branchiogenic cyst
- lymphangioma
- hemangioma
- dermoid cyst

Inflammatory lesions
- lymphadenopathy
- salivary gland disease
- thyroid disease

Neoplastic lesions
- lymphadenopathy
- tumors of the salivary glands
- tumors of the thyroid gland
- carotid body tumor
- lipoma
- fibroma
- other soft-tissue tumors

Miscellaneous
- tumors of the skin and dermal appendages
- ranula
- vascular anomalies
- tumors arising from bone
- muscular deformities

Despite the advanced technology in medicine, the clinician still can effectively rely on the information obtained from a detailed history and physical examination. These may define the characteristics and location of the mass, in order to arrive at a differential diagnosis that includes just a few possibilities. Each clinical diagnosis however, will be associated with some uncertainty: this is due to the multitude of structures in the neck, the limited capacity of palpation to discern solid and cystic lesions, and the difficulties in defining exact anatomic relationships. In a muscular, short, scarred or adipose neck physical examination is further compromised. Furthermore, it is impossible to differentiate between benign and malignant disease, or to predict a histological classification on a clinical basis.

The difficulties in evaluating head and neck masses actuated the present study, which started in 1984. By that time small-parts ultrasound transducers had been developed. These high-frequency transducers seemed more suitable for examination of the superficial tissues in the head and neck region than earlier ultrasound equipment. In close cooperation between the department of Radiology and the department of Otorhinolaryngology and Head and Neck Surgery, a prospective study on the value of ultrasound examination of the head and neck was designed. The purpose of this study was to determine the value of ultrasound examination in the evaluation of head and neck masses. A second purpose of this study was to appraise the adjunctive value of cytologic examination in the above mentioned clinical problems.

Patients and methods

Palpation

All patients with an evident or suspected mass in the neck who were referred to the department of Otorhinolaryngology, were examined by an experienced head and neck surgeon (P.C. de Jong M.D., Ph.D, P. Knegt M.D., Ph.D., E.J. v.d.Schans M.D. and G.J. Gerritsen M.D., Ph.D.). Following history taking and a complete ENT-examination, the neck mass was examined.
All lesions were judged on exact localization, size, consistency, moveability and extension. The overlying skin was examined for fistula and signs of inflammation. Tenderness was recorded. The rest of the neck was screened for lymph nodes and other pathology.

Physical examination of the parotid gland included inspection of Stensen's duct orifice, soft palate and lateral pharyngeal wall. Facial nerve function was noted. The transverse process of the second cervical vertebra was identified.
The submental and the submandibular regions were examined bimanually. Attention was directed to Whartin's duct, the submandibular gland and the regional lymph nodes.

Masses in the lateral portions of the neck were examined for multiplicity, expansion during Valsalva's manoeuvre, pulsations and bruits. Special attention was given to the relationship of the lesion to the sternocleidomastoid muscle and the carotid artery.
Lesions in the midline of the neck were checked for expansion during Valsalva's manoeuvre. The patient was asked to swallow while palpation was in progress. The tongue and larynx were evaluated for abnormalities near the foramen cecum and for intralaryngeal masses. Relationship to the laryngeal skeleton and the thyroid gland were established.

Ultrasound examination

Ultrasound examination was performed without knowledge of the clinical history, the results of physical examination or any other diagnostic test. Through this design, every lesion was examined by the sonographer as if it were an elusive head and neck mass.
Ultrasound examination was performed by the authors (RJR and RJBdJ), or in the absence of the authors, by the head of the department of ultrasound (J.S. Lameris M.D., Ph.D. (JSL)). From October 1987 the ultrasound examinations were performed by a resident (H. van Overhagen M.D. (HvO)) who had a special interest in ultrasound examination of the head and neck region.
The ultrasound examinations were performed with Philips and Aloka equipment (Philips 1500, Aloka 280 and 650) using 5.0 and 7.5 MHz small-parts transducers.
The patient was examined in a supine position with slight extension of the neck allowing a good approach of the transducer. A gel was applied to the skin in order to improve contact with the transducer.

Other diagnostic tests

Other investigations (e.g. cytologic examination, CT, sialography, conventional tomography) were performed when indicated clinically.
For cytologic examination the same technique as described in the Introduction of Part II was used. The smear was examined by an experienced cytopathologist (D.I. Blonk, M.D., Ph.D. and R. van Pel M.D., Ph.D).
CT was performed with a Philips Tomoscan 350. Dependent on the clinical information and the extent of the mass by palpation, 3 to 6 mm scans were made with the gantry parallel to the hard palate. Coronal sections and intravenous contrast medium were used when indicated. The scans were interpreted by a senior radiologist (A.I.J. Klooswijk, M.D.), and reviewed independently by one of the authors (RJR).
Sialography and conventional tomography were assessed by residents under supervision of a staff radiologist. The pictures were reviewed by the authors (RJR and RJBdJ).

Findings of palpation, ultrasound, CT and operative findings were recorded in a diagram (appendix A).

The results of ultrasound examination were compared to the results of other investigations, and to operative and histopathologic findings, when available.
Initially, ultrasound was performed in addition to the usually applied diagnostic modalities. During the study the values and limitations of ultrasound examination in the diagnostic work-up of patients with a head and neck mass became clear. As a result of the positive contribution of ultrasound examination, other methods of investigation were abandoned, leading to a different strategy in the diagnostic work-up of a lump in the neck. This change in diagnostic modalities accounts for the fact that not all methods of investigation were performed in all patients.

Selection of patients

The patients were selected for evaluation in two different ways:

- on the basis of the ultrasound diagnosis as mentioned in the radiological reports. The ultrasound diagnosis was compared to the final diagnosis as recorded in the records of the patient. In this way the true-positive and false-positive results of ultrasound were traced.

- on the basis of diagnostic data in the data-system of the University Hospital and/or the files of the surgical ward of the department of Otorhinolaryngology and Head and Neck Surgery. In the data-system of the hospital all diagnoses for each patient are listed and in the files of the surgical ward all operations are recorded. It was checked for the conditions which will be discussed in part III, whether these patients have had an ultrasound examination and if so, the ultrasound diagnosis was compared to the final diagnosis. This was to identify the false-negative results of ultrasound examination. As a consequence of this design, true-negative results of ultrasound examination are not included in this study.

The studies which are presented in part III comprise approximately 150 patients. Many more patients were examined by ultrasound, but several subsets of patients were not included:
- patients with thyroid disease;
- patients who were referred from other departments;
- patients who were not examined by one of the previously mentioned participants of the study;
- patients in whom the pathology which was suspected clinically, was excluded on the basis of negative ultrasound findings.

The commonest causes of head and neck masses are discussed in the next chapters. Chapter III.1 deals with the value of ultrasound examination in thyroglossal duct anomalies. In chapter III.2 the place of ultrasound and cytologic examination in the diagnostic work-up of patients with branchiogenic cysts is described. The ultrasound findings in patients with a laryngocele are presented in chapter III.3. In chapter III.4 a comparison is made between palpation, CT and ultrasound examination in localizing tumors of the parotid gland. Chapter III.5 reports on the ultrasound characteristics of the commonest parotid gland tumors. Furthermore, the value of ultrasound examination and (UG-)FNAB in differentiating between benign and malignant disease is appraised. The changes seen in inflammatory disease of the salivary glands as well as the possibility to detect calculi and dilated ducts are presented in chapter III.6. In chapter III.7 the contribution of ultrasound examination to the diagnosis and assessment of cervical tuberculous adenitis is evaluated. The ultrasound appearance of the dermoid cyst, cystic hygroma, carotid body tumor, aneurysm of the carotid artery, the ranula, deformity of the cervical spine, and masseteric hypertrophy are presented in chapter III.8. In the comment (chapter III.9), the value of ultrasound in the assessment of head and neck masses is estimated. A guideline for the use of ultrasound is given in the addendum of part III.

Chapter III.1

Ultrasound characteristics of thyroglossal duct anomalies

Abstract

The purpose of this study was to determine the value of ultrasound examination in the diagnosis of thyroglossal duct anomalies. The ultrasound and palpation findings in 24 patients with a thyroglossal duct anomaly were reviewed. Cysts, tracts and ectopic thyroid tissue appeared to produce a characteristic ultrasound pattern in most cases.
This study includes 5 patients with non-symptomatic lesions which were detected at ultrasound examination.
The necessity of performing a radionuclide scan prior to surgery for a thyroglossal duct anomaly is reconsidered in view of the diagnostic power of ultrasound in thyroid disease.

Introduction

Thyroglossal duct anomalies are midline defects that arise from failure of complete obliteration of the thyroglossal duct. The thyroglossal duct is an epithelium-lined tube that begins its development in the 3rd or 4th embryonic week in the floor of the pharynx. At this site, which later becomes the foramen cecum, the thyroid gland is initially developed. The thyroid gland descends from the floor of the pharynx through the anterior midline of the neck to reach its final position ventro-caudal to the thyroid cartilage by the end of the 7th week. During its descent the gland remains connected to the floor of the pharyngeal gut by means of the thyroglossal duct. As the hyoid arch is formed by bilateral "anlages" which unite in the midline, the thyroglossal duct may become entrapped, resulting in the duct lying within the periosteum of the hyoid bone or even passing through its bony substance.
The thyroglossal duct usually atrophies and disappeares between the 5th and 10th week. At any point along the migratory path of the thyroid gland, a remnant of epithelial cells can persist, causing the formation of a cyst, a fistula or ectopic thyroid gland tissue.
Thyroglossal duct cysts are the most common thyroglossal duct anomalies, and the most common non-odontogenic cysts in the head and neck region. They are seen in equal frequency in men and women in their second and third decades, but may be identified at any age. Thyroglossal duct cysts are round, smooth masses that in most cases move with swallowing and tongue protrusion. They are usually asymptomatic but may become infected during an upper respiratory tract infection. Following abscess formation with discharge a fistula may result.
Differential diagnostic considerations of midline cervical masses are lymphadenopathy, medially placed branchial cyst, laryngocele, dermoid cyst, ectopic thyroid tissue, lipoma and sebaceous cyst.
Before the advent of CT and ultrasound examination, the commonly used radiological tests to evaluate a mass in the neck were conventional soft-tissue radiographs and radionuclide

scanning. These latter tests proved to be of little value. Recently CT has been advocated for further assessment of thyroglossal duct anomalies. CT may provide an accurate delineation of the localization of a thyroglossal duct cyst, its size and character, as well as its relationship to surrounding structures[1 2].
In general, ultrasound examination is recommended for its capacity to distinguish between solid and cystic lesions [3 4 5]. However, there are no detailed reports on the accuracy of ultrasound to assess thyroglossal duct anomalies.
In this study we have evaluated the value of ultrasound examination in thyroglossal duct anomalies by reviewing 24 patients with this diagnosis. The place of ultrasound in the diagnostic work-up of patients with thyroglossal duct anomalies is defined.

Patients and methods

Between December 1984 and December 1988, all patients who presented to the department of Otorhinolaryngology with an evident or suspected lump in the neck were independently examined by an experienced head and neck surgeon (palpation) and a sonographer.
All patients with an ultrasound diagnosis of thyroglossal duct anomaly, and patients with a histologically and/or CT-proven anomaly were reviewed. Twenty-four patients were available for evaluation. There were 17 cysts, 2 non-palpable recurrences, and 5 non-palpable coincidental findings at ultrasound examination. The palpable lesions were confirmed by histopathologic examination (9 cases) or CT (8 patients). The non-palpable lesions (7 cases) were not verified.
The results of the ultrasound examination in palpable lesions were compared with the results of palpation.

Results

Palpation

In 17 patients the histopathological and/or CT diagnosis was thyroglossal duct anomaly. Fourteen of these 17 patients were correctly identified by palpation (true positive results). The clinical diagnosis was incorrect in 3 patients: two lesions were mistaken for a laryngocele and one was erroneously interpreted as a lymph node (false negative results). The latter 3 patients were correctly assessed at ultrasound examination. No false positive results of palpation were recorded.

Ultrasound findings in patients with palpable masses

In 15 of 17 histologically or CT-proven cases of thyroglossal duct anomaly, the ultrasound diagnosis was correct (true positive results). A round to ovoid shaped low echogenic lesion with a bright well-defined capsule and posterior acoustic enhancement was demonstrated in these cases. In most patients a close relationship to the hyoid bone (8 patients) (fig. 1) or a

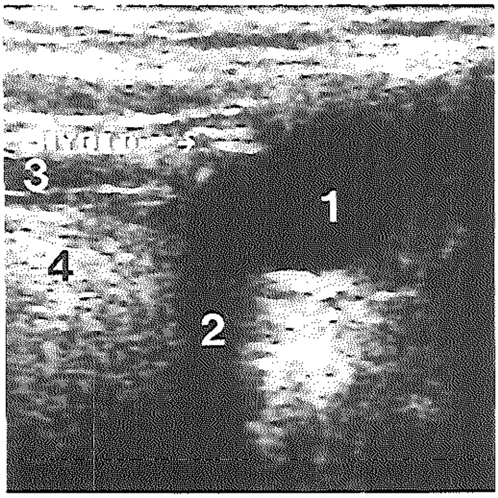

Fig. 1 *Longitudinal section in the midline at the level of the hyoid bone. The close relationship of a thyroglossal duct cyst to the hyoid bone is shown. The cyst presents as an echo-free structure with posterior acoustic enhancement.*
1 well-defined cyst
2 posterior acoustic shadowing of hyoid bone
3 mylohyoid muscle attached to hyoid bone
4 base of the tongue

fistulous tract was depicted (3 patients) (fig. 2). In two patients both findings were apparent at ultrasound examination. In one patient a cystic mass with a small and strongly echogenic part in it was demonstrated. Ultrasound guided fine needle aspiration biopsy (UGFNAB) confirmed the presence of ectopic thyroid tissue in a thyroglossal duct cyst in this particular patient. The ultrasound characteristics of thyroglossal duct anomalies are summarized in Table 1.

Table 1 Ultrasound characteristics of thyroglossal duct anomalies

* round or ovoid shaped lesions
* generally of low echogenicity
* well-defined capsule
* posterior acoustic enhancement
* often a close relationship to the hyoid bone
* sometimes with a fistulous tract to the base of the tongue or the skin.

In 2 patients an echogenic mass, cranial to the hyoid bone and without a tract, was demonstrated. Ultrasound diagnosis was dermoid cyst in these patients. Histopathologic examination however demonstrated a thyroglossal duct cyst; these 2 patients were false negative results of ultrasound examination. There were no false positive results.

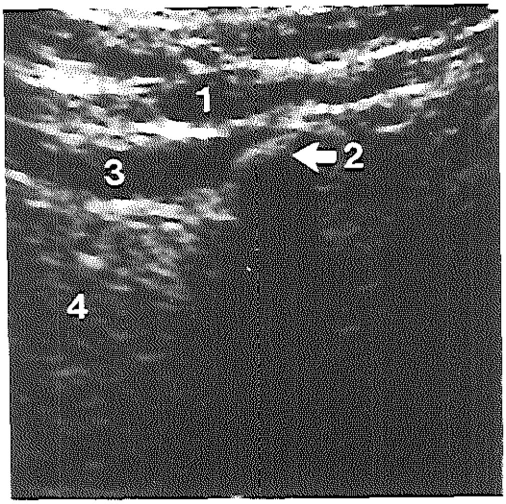

Fig. 2 *Longitudinal section lateral in the neck at the level of the hyoid bone. A fistulous tract, characterized by low echogenicity, is located superficial to the hyoid bone.*
1 fistulous tract
2 hyoid bone
3 muscles of the floor of the mouth
4 base of the tongue

Non-palpable recurrences after surgery for thyroglossal duct cysts

Two patients were referred to the radiologist for ultrasound examination because of globus complaints after a simple cystectomy. These patients had no palpable pathology. Ultrasound examination revealed small recurrences at the hyoid bone. These recurrences were small cysts. A CT or histopathological verification of these findings was not available.

Non-palpable coincidental findings

In 5 patients ultrasound examination was performed in the diagnostic work-up of patients with other lesions in the head and neck region. These patients had no complaints of a thyroglossal duct anomaly whatsoever, and their depiction was coincidental. Four of these patients showed a persisting duct in the base of the tongue (fig. 3); in the other patient a small cyst, closely related to the hyoid bone, was demonstrated (fig. 4). These findings were not verified.

In all patients a thyroid gland was visualized in the usual place.

Discussion

In this study, the diagnostic value of palpation and ultrasound examination in the evaluation of patients with a midline cervical mass were essentially similar. The pathognomonic relation to the hyoid bone may be anticipated at palpation, but can be demonstrated by ultrasound. Unlike clinical examination, ultrasound can reveal a fistulous tract in the base of the tongue.

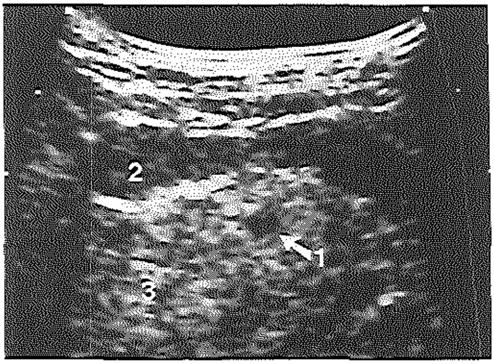

Fig. 3a *Tranverse view of the floor of the mouth and the base of the tongue. A small, well-defined, low echogenic structure, based on a thyroglossal duct is present in the base of the tongue.*
1 duct
2 muscles of the floor of the mouth
3 base of the tongue

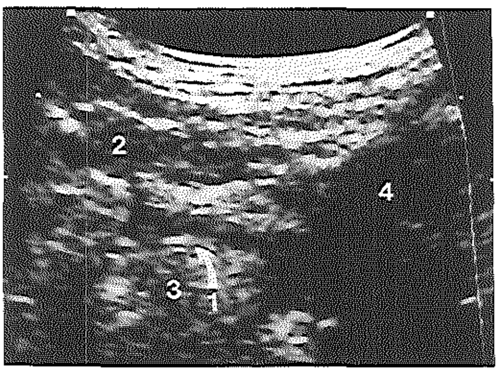

Fig. 3b *Longitudinal view of the base of the tongue, in the midline, presenting the same duct as in Fig. 3a.*
1 duct
2 muscles of the floor of the mouth
3 base of the tongue
4 hyoid bone

These tracts may ascertain the diagnosis.
The patients who where incorrectly assessed at ultrasound examination (2 patients) differed from the patients misjudged at palpation. This suggests that positive findings of palpation and ultrasound are confirmatory. When the findings differ from each other, conclusive value may be attached to the ultrasound depiction of a close relation to the hyoid bone or a fistulous tract. When these findings are not apparent, or when the lesion is echogenic, cytologic examination may provide additional information[6].

The depiction of 2 non-palpable recurrences after surgical treatment and the demonstration of 5 non-palpable coincidental findings, are suggestive of a higher sensitivity of the ultrasound examination when compared to palpation. The coincidental findings indicate that thyroglossal duct anomalies may be more common than is usually assumed.

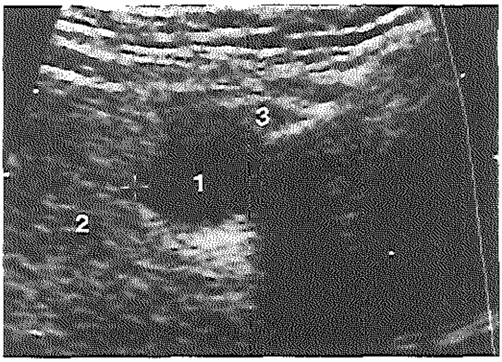

Fig. 4 *Longitudinal section, in the midline, at the level of the base of the tongue and the hyoid bone. Coincidental finding of a small thyroglossal duct cyst just cranial to the hyoid bone. The cyst presents as a moderate defined, low echogenic structure with posterior acoustic enhancement.*
1 thyroglossal duct cyst
2 base of the tongue
3 hyoid bone

Thyroid isotope scans prior to surgery are usually advocated in order to identify all functioning thyroid tissue[7 8]. This is to reduce the risk that the only functioning thyroid tissue would be removed, when the anomaly is excized, resulting in the patient being hypothyroid. Ultrasound examination may be used for identification of the thyroid gland: it is very unlikely that a thyroid gland with a normal parenchymal pattern, demonstrated at ultrasound examination, would be non-functioning. Therefore, we suggest that in case of thyroglossal duct anomalies ultrasound examination should be extended to the lower neck, in order to identify thyroid tissue other than in the anomaly to be removed.

Conclusions:

1. A thyroglossal duct cyst is characterized by a round to ovoid shape, low echogenicity, a bright well-defined capsule and posterior acoustic enhancement.
2. A close relationship of a mass with the hyoid bone and/or depiction of a tract in the base of the tongue, strongly suggests the diagnosis of a thyroglossal duct anomaly.
3. Thyroglossal duct anomalies are accurately assessed by ultrasound, although dermoid cysts may cause differential diagnostic problems.
4. In patients with complaints after surgery for a thyroglossal duct cyst, ultrasound may reveal a non-palpable recurrence.
5. Ultrasound examination may demonstrate non-palpable thyroglossal duct anomalies which are non-symptomatic, suggesting that these lesions are more common than is usually assumed.
6. Visualization of a normal thyroid gland at ultrasound examination, renders a thyroid isotope scan superfluous.

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Chapter III.2

Evaluation of branchiogenic cysts by ultrasound examination

Abstract

Ultrasound and palpation findings of seventeen patients with branchiogenic cysts were studied. Results were compared with operative and histopathologic findings in 13 patients, and to fistulography, cytologic examination and/or CT in 4 patients.
Ultrasound findings (appearance, location and extension) were characteristic in 15 of 17 cases. Palpation proved to be incorrect or inconclusive in more than half of the patients.
It is concluded that ultrasound examination of the neck may contribute to the correct pre-surgery diagnosis of branchiogenic cysts.

Introduction

Branchiogenic anomalies result from incomplete obliteration of the branchial clefts, arches and pouches. Lesions may take the form of cysts, sinuses or fistulas. Branchiogenic cysts, fistulas and sinuses occur with equal frequency in males and females. They may be bilateral and familial tendencies have been noted. Cysts are rarely diagnosed at birth but become apparent in late childhood or adulthood. They can occur anywhere along the anterior border of the sternocleidomastoid muscle from the external auditory canal and/or parotid gland to the lower neck. The usual clinical presentation is a round, non-tender, mobile, fluctuant mass, 3 to 5 cm in diameter. Fluctuations in size with episodes of inflammation, often associated with upper respiratory infections, may be seen. Infected cysts may develop into abscesses, which may spontaneously rupture, forming a draining sinus. Fistulas and sinuses usually present as a small opening along the anterior border of the sternocleidomastoid muscle. The pinhole orifice may discharge material, which may be milky, serous, mucoid or purulent.
The differential diagnosis of branchiogenic cysts may be difficult, since a variety of lesions (e.g. cystic hygroma, laryngocele, lymph nodes, (epi-)dermoid cyst, salivary gland lesions) have to be taken into account.

CT and ultrasound examination have been advocated for the assessment of branchial cleft anomalies. CT can provide an accurate delineation of the neck mass, its size and character, as well as its relationship to surrounding structures[1] (fig. 1). Ultrasound examination may distinguish between solid and cystic lesions[2,3,4,5].
In this study, the contribution of ultrasound examination to the diagnosis and the assessment of branchiogenic cysts was retrospectively evaluated and compared to the results of expert palpation.

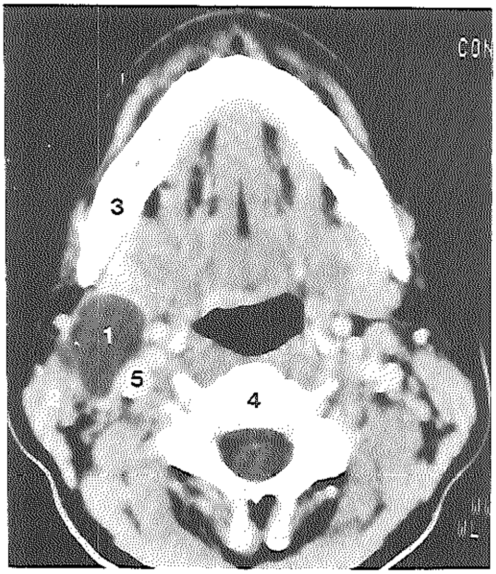

Fig. 1 *CT section at the level of the second cervical vertebra parallel to the mandible. A well-defined branchiogenic cyst at the anterior border of the sternocleidomastoid muscle is demonstrated.*
1 branchiogenic cyst
2 sternocleidomastoid muscle
3 mandible
4 vertebra
5 carotid artery

Patients and methods

Between December 1984 and December 1988, all patients who presented in the Department of Otorhinolaryngology with a lump in the neck were examined independently by an experienced head and neck surgeon (palpation) and a sonographer, prior to surgery.
Records and sonograms of 17 patients with a branchiogenic cyst were reviewed.
The results of the ultrasound examination and palpation in 13 patients, were compared with the operative and the histopathologic findings. Four patients were not operated, because they had few complaints, refused surgical treatment, or were not fit for general anaesthesia. The definite diagnosis in these 4 patients was established by fistulography (1 patient), CT (1 patient) and cytologic examination (2 patients).

Results

The masses were found at the anterior border of the sternocleidomastoid muscle (fig. 2), and were round to ovoid shaped. The results of palpation and ultrasound examination are listed in Table 1.

Palpation

Palpation resulted in the correct diagnosis of a branchiogenic cyst in 8 patients. Five palpable masses were mistaken for lymph nodes and 2 for lipomas. In the remaining 2 patients no clinical diagnosis could be established.

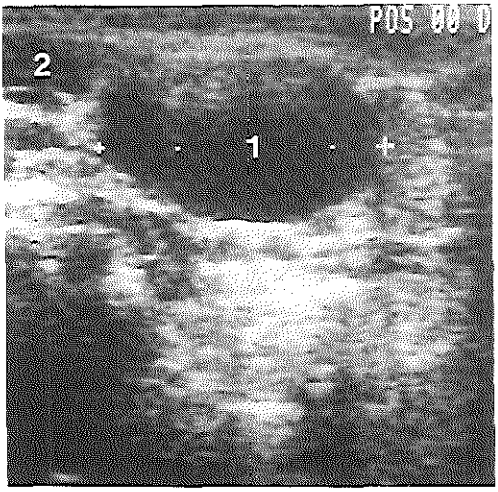

Fig. 2 *Transverse view of the right side of the neck. A branchiogenic cyst, which presents as a low echogenic mass with well-defined borders and posterior acoustic enhancement, is located at the anterior border of the sternocleido-mastoid muscle.*
1 cyst
2 sternocleidomastoid muscle.

Table 1 Results of palpation and ultrasound in 13 patients with a histopathologically proven branchiogenic cyst. In an additional group of 4 patients (patients 14, 15, 16, and 17), no histopathologic examination was available. In these patients the results of fistulography, CT and cytology were used to establish the definite diagnosis.

PATIENT	PALPATION	ULTRASOUND	METHOD OF VERIFICATION
1	lipoma	cyst	histopathology
2	cyst	cyst	histopathology
3	no diagnosis	lymph node	histopathology
4	cyst	cyst	histopathology
5	lymph node	cyst	histopathology
6	lymph node	cyst	histopathology
7	cyst/fistula	cyst/fistula	histopathology
8	no diagnosis	cyst	histopathology
9	lymph node	cyst	histopathology
10	lymph node	cyst	histopathology
11	lipoma	lymph node	histopathology
12	cyst	cyst	histopathology
13	cyst	cyst	histopathology
14	lymph node	cyst	cytology
15	cyst	cyst	CT
16	cyst/fistula	cyst/fistula	fistulography
17	cyst	cyst	cytology

Ultrasound examination

All lesions were visualized lateral to the carotid artery and jugular vein (fig. 3a). A bright well-defined border and posterior acoustic enhancement was demonstrated in 15 of 17 patients. These lesions had variable internal echoes, and were diagnosed as branchiogenic

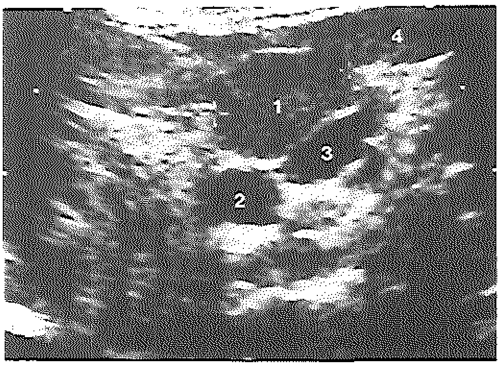

Fig. 3a *Transverse view of the left side of the neck. A branchiogenic cyst with solid appearance is located superficial to the common carotid artery and the jugular vein.*
1 branchiogenic cyst
2 common carotid artery
3 jugular vein
4 sternocleidomastoid muscle

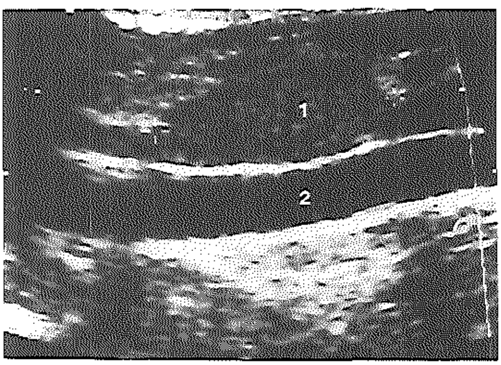

Fig. 3b *Longitudinal view of the same branchiogenic cyst as in Fig. 3a.*
1 branchiogenic cyst
2 common carotid artery

cysts by the sonographer. The remaining 2 masses had a highly echogenic appearance, and no capsule or posterior acoustic enhancement was demonstrated. These lesions were interpreted as being lymph nodes (false negative results) (fig. 3b).

In 5 of 17 cases ultrasound examination demonstrated a cranial extension of the lesion behind the tail of the parotid gland. In 2 other patients, a fistula was visualized as a medial extension of the lesion in the direction of the tonsillar fossa (fig. 4). One patient with a medial fistula had a fistulous tract into the skin as well and the ultrasound findings were confirmed at fistulography. The medial fistula in the second patient was confirmed at surgery.

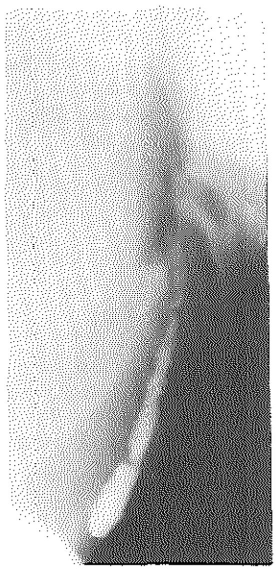

Fig. 4a *Lateral X-ray view of the neck. Fistulogram depicting a branchiogenic fistulous tract from the level of the thyroid gland to the tonsillar fossa cranially.*

There were no false positive results of the ultrasound examination. False negative results of ultrasound examination were traced by checking the data-bases, as mentioned in the introduction of Part III. Negative results of ultrasound examination were generally not verified, because patients with a negative result were less likely to be referred for surgery.

Cytology

Cytologic examination was performed in 11 patients. In 9 of these patients, the cytologic diagnosis of a branchiogenic cyst was confirmed at histopathologic examination. The descriptions of all cytologic examinations mentioned amorphous debris, cholesterol crystals, benign squamous epithelium, and/or lymphocytes.
Nine of the 11 aspirations were performed by the clinician because there was doubt concerning the clinical diagnosis. These included the two lesions, interpreted at ultrasound as being lymph nodes. The cytologic diagnosis permitted a correct pre-surgery diagnosis in the cases misinterpreted at ultrasound. In the remaining 2 patients, the cytologic diagnosis was not verified.

Discussion

Branchiogenic cysts have to be differentiated from a variety of lateral cervical lesions. This may be difficult on grounds of clinical examination alone. In 9 of 17 patients, palpation did not lead to a correct diagnosis, probably because the cystic nature was not apparent at palpation. In the remaining 8 patients the cystic nature, history and location of the mass produced the correct diagnosis. In large series in literature a similar reliability of clinical pre-

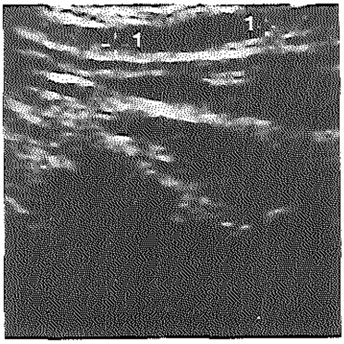

Fig. 4b *The ultrasound presentation of the same fistulous tract as shown in fig. 4a. Longitudinal view of the cystic dilatation of the most caudal part of the fistula.*
1 fistula

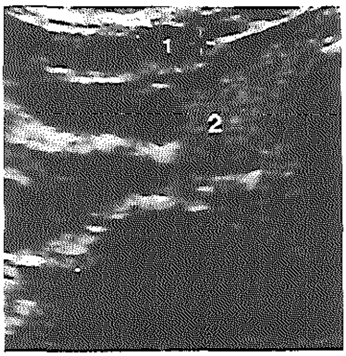

Fig. 4c *Transverse view of the cystic dilatation of the most caudal part of the fistula.*
1 fistula
2 thyroid gland

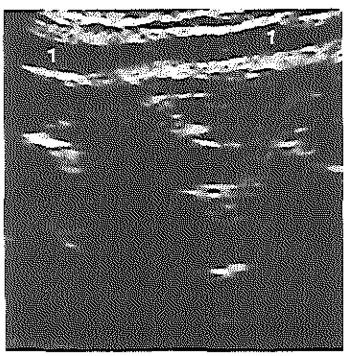

Fig. 4d *Middle third of the fistula, demonstrated as a low echogenic tubular structure. Longitudinal view.*
1 fistulous tract

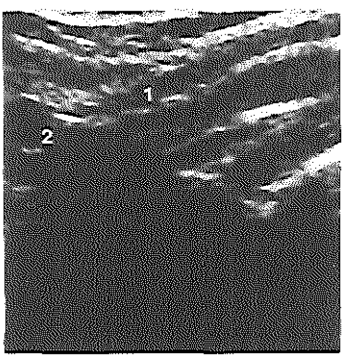

Fig. 4e *Fistula ending in the tonsillar fossa. Longitudinal view.*
1 fistula
2 tonsillar fossa

operative diagnosis was reported: 50-60%[6 7 8].
The ultrasound appearance of branchiogenic cysts appeared to be fairly characteristic in our patients. All lesions were visualized at the anterior border of the sternocleidomastoid muscle and lateral to the carotid artery. Depiction of a cranial extension and/or a fistula can be explained by the embryologic derivation of branchial cleft anomalies, and seems to be pathognomonic for these lesions. These findings concerning extension, fistulas and relationship to surrounding structures may influence surgical approach.
The majority of the lesions exhibited the typical ultrasound features of a cyst: depiction of a wall and posterior acoustic enhancement. It must be stressed, however, that echogenicity varied from anechogenic to highly echogenic. This is probably due to the variable quantities of mucus, cholesterol crystals, debris, lymphocytes and epithelial cells inside branchiogenic cysts. With advanced high-frequency transducers, these contents are nowadays visualized, whereas earlier equipment failed to do so and all branchiogenic cysts were considered to be echo free. Actually, high echogenicity in two of the cysts led to the erroneous interpretation of lymph nodes. Little or no difference in echogenicity of the contents of the cyst, its wall and the surrounding tissues, explains the absence of posterior acoustic enhancement and the absence of a capsule and, therefore, the resemblance to solid lesions. Pre-surgery differentiation from solid lesions in these cases was established by cytologic examination.
The results of cytologic examination in our study correlated well with histopathology. Engzell[9] however, found an accuracy-rate of 86% in the establishment of branchiogenic cysts. There are several possible explanations for lower accuracy-rates. In the first place, the aspirate may not be taken from the lesion, but from adjacent structures. Secondly, just the wall of the cyst may have been aspirated. Smears will show lymphatic or epithelial cells only, which might cause confusion with lymphatic or salivary gland tissue. In addition, aspiration from the contents of the cyst only, may show neither cells nor cholesterol crystals, not allowing definitive conclusions. Finally, aspirations of cystic, squamous cell carcinoma metastases may resemble the cytologic appearance of branchiogenic cysts. Therefore, the 2 aspirations which were not verified, may have been from nodal metastases. However, the clinical course in these patients, who were not treated surgically, indicated a benign lesion.

In summary

1 The conclusions at clinical examination proved to be incorrect or inconclusive in more than half of the patients with a branchiogenic cyst.
2 The ultrasound appearance of a branchiogenic cyst is an encapsulated lesion with posterior acoustic enhancement and a variable amount of internal echoes at the anterior border of the sternocleidomastoid muscle. When a lateral cervical mass is not completely echo free, cytologic examination permits differentiation from solid lesions.
3 Depiction of a fistula or cranial extension is pathognomonic.

Conclusion

Ultrasound examination (with cytologic examination when required) may lead to a correct diagnosis in branchiogenic cysts. In addition, ultrasound examination may supply data concerning extension, fistulas and relationship to adjacent structures which may influence surgical approach.

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Chapter III.3

Ultrasound examination in the diagnosis of laryngoceles

Abstract

Clinical and anatomical features of laryngoceles are reviewed. Furthermore, the ultrasound characteristics of 8 patients with laryngoceles are outlined. Internal laryngoceles appeared to be echo free, well-defined structures inside the thyroid cartilage. Combined laryngoceles had an additional cystic mass outside the laryngeal skeleton, at the thyrohyoid membrane. Characteristically, this cystic mass was connected through the thyrohyoid membrane to the intra-laryngeal mass. Finally, the value of ultrasound examination in the diagnostic work-up of patients with laryngoceles is appreciated and compared to the respective values of ENT-examination, conventional tomography and CT.

Introduction

The laryngocele was first reported by Larrey[1], surgeon to Napoleon's army in Egypt, in 1829. He described compressible pouches related to the thyrohyoid membrane in the Muezin, who called the faithful to prayer from the minarets and he described these swellings as 'goitres aeriennes'.

At present, laryngoceles are considered to be dilatations of the saccule of the laryngeal ventricle of Morgagni. These lesions are quite rare: reviewing the literature, Stell[2] calculated an incidence of 1 per 2,500,000 per annum in Great Britain. Canalis[3] recorded 300 cases of proven laryngoceles in the world literature in 1977.

Laryngeal tumor[2,3], hobbies and occupations requiring blowing[3,4] seem to be important etiological factors. As the length of the saccule varies in normal larynges, a congenitally long saccule may be an important factor in the pathogenesis of laryngoceles as well (usually the laryngeal ventricle does not extend above the upper border of the thyroid cartilage).

Laryngoceles are classified as internal when limited to the internal larynx, as external when present in the neck and communicating with an undistended saccule, and as combined when a sac both medial and lateral to the larynx is present. The combined type is the commonest and the internal type is second in frequency.

The most common presenting symptoms are hoarseness and a swelling in the neck. Stridor, dysphagia, sore throat, snoring, pain or coughing are less frequent symptoms. Complications of the lesions are airway obstruction, pyocele formation or, quite rare, vocal cord paralysis and subcutaneous emphysema.

Diagnosis is by ENT-examination, contrast laryngograms, conventional tomography and computed tomography. Neoplasms and intralaryngeal cysts have to be differentiated from internal laryngoceles. External and combined laryngoceles may resemble branchiogenic cysts and lymph nodes in clinical appearance.

Small asymptomatic laryngoceles require no therapy because they seldom produce any difficulty. Symptomatic laryngoceles of any size and those that are infected should be excised. Marsupialisation by CO2-laser or microlaryngoscopic techniques is advocated for small internal laryngoceles. Larger internal, all external and combined laryngoceles should be removed using a lateral pharyngotomy approach.

In the present study ultrasound characteristics of laryngoceles are discussed and the place of ultrasound examination in the diagnostic work-up of this anomaly is defined.

Patients and methods

Between December 1984 and December 1988, 12 patients with a laryngocele were seen in the University Hospital Rotterdam. In 8 patients ultrasound examination of the neck was performed. These patients are the subject of this study. The ultrasound examination was performed by a sonographer who had no knowledge of the clinical data.
ENT-examination was performed in all; CT and/or conventional tomography in 6 patients. Definitive diagnosis was ascertained by endoscopy and/or surgery.
Records, reports of the ultrasound examination, sonograms and radiograms were reviewed.

Results

The results are summarized in Table 1. Three patients had an internal laryngocele; in 5 patients a combined type was established. There were no patients with an external laryngocele.

Physical examination (n=8)

Physical examination produced the correct diagnosis in 5 patients; in 1 patient a thyroglossal duct cyst was diagnosed erroneously, and in another no definite diagnosis could be made. The larynx of the remaining patient was obscured by a retropharyngeal abscess at intake.

Table 1 Results of physical examination, ultrasound examination, CT and conventional tomography in 8 patients with laryngoceles.

	CORRECT	INCORRECT	INCONCLUSIVE	NOT PERFORMED
PALPATION	5	1	2	-
UTRASOUND	8	-	-	-
CT	5	1	-	2
CONVENTIONAL TOMOGRAPHY	1	-	5	2

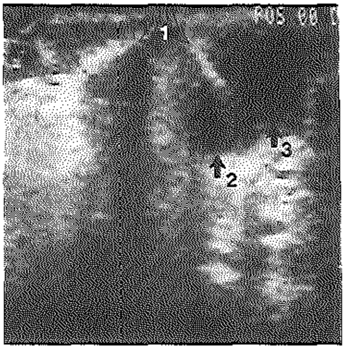

Fig. 1a *Transverse sonogram in the midline of the neck demonstrating the thyroid cartilage (open arrows) and a laryngocele of the combined type (closed arows).*
1 thyroid cartilage
2 internal part of the laryngocele
3 external part of the laryngocele

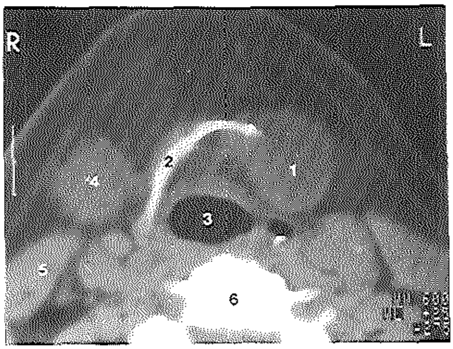

Fig. 1b *Transverse CT view at the level of the hyoid bone of the same patient. The laryngocele is clearly demonstrated as a fluid filled, encapsulated structure adjacent to the hyoid bone.*
1 laryngocele
2 hyoid bone
3 air in the larynx
4 submandibular gland
5 sternocleidomastoid muscle
6 vertebra

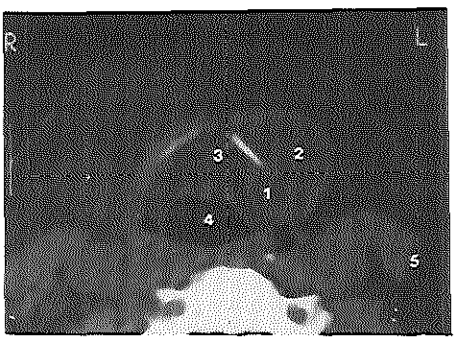

Fig. 1c *Transverse CT section at the level of the thyroid cartilage in the same patient.*
1 internal part of the laryngocele
2 external part of the laryngocele
3 thyroid cartilage
4 air in the larynx
5 sternocleidomastoid muscle

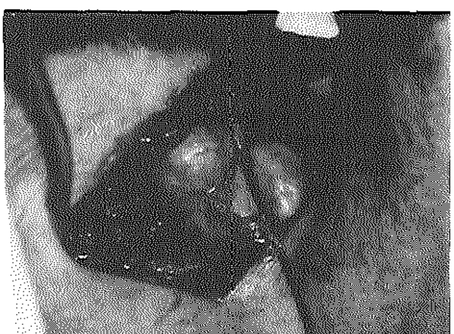

Fig. 1d *At surgery the ultrasound findings were confirmed (the connecting part of the laryngocele is in a vessel-loop).*

Ultrasound examination (n=8)

All lesions were accurately diagnosed by ultrasound. Internal laryngoceles appeared to be echo free, well-defined structures inside the thyroid cartilage. In patients with the combined type, cystic masses at the thyrohyoid membrane, connected to the intralaryngeal part, were depicted (fig. 1).
No false-positive results of ultrasound examination were encountered: all cystic intra-laryngeal lesions appeared to be laryngoceles. When solid, intra-laryngeal masses were carcinomas in our experience.

CT (n=6)

In 5 of 6 patients CT showed a laryngocele. The laryngoceles were characterized by well-defined margins, densities indicating liquid contents, and a localization inside the thyroid cartilage, or at the level of the thyrohyoid membrane (fig. 1). In 1 patient the laryngeal cyst, as interpreted on grounds of CT, proved to be an internal laryngocele at endoscopy.

Conventional tomography (n=6)

In 5 of 6 patients an intralaryngeal mass was visualized by conventional tomography. As a consequence of the liquid contents, the laryngoceles presented as soft tissue masses and were erroneously considered to be of neoplastic origin (fig. 2). None of our patients had cancer of the larynx. In one patient conventional tomography adequately demonstrated a laryngocele.

Fig. 2 *At conventional tomography a laryngocele appeared as a soft tissue mass (arrows).*

Discussion

Usually, CT and conventional tomography are performed in the evaluation of laryngoceles. Only few studies deal with the evaluation of (intra-)laryngeal structures by real-time ultrasound[5 6 7]. Ultrasound is hampered by the (partly) mineralized cartilage of the larynx and the air in the air-way. As most sound waves are reflected at interfaces with cartilage or air, intralaryngeal structures are obscured. Recent studies however[5 6 7], clearly demonstrated that ultrasound may visualize e.g. thyroid cartilage invasion and advanced laryngeal cancer. The present study is to our knowledge the first to describe the sonographic appearance of laryngoceles.

The ultrasound features of both the internal and combined type appeared to be quite specific. A fluid-filled laryngocele presents as an echo free, well-defined structure inside the margins of the thyroid cartilage (internal laryngoceles), and at the level of the thyrohyoid membrane in laryngoceles of the combined type. The recognition of air-filled laryngoceles is probably more difficult due to the presence of strong reflections caused by the air, which may be confused with air in the larynx.

Lateral cystic masses may be branchiogenic cysts or laryngoceles. The exact localization of the lesion and the depiction of a communication through the thyrohyoid membrane appeared to be characteristic ultrasound features of laryngoceles. In chapter III.2, branchiogenic cysts were demonstrated to produce a quite different ultrasound pattern: encapsulated lesions with posterior acoustic enhancement and a variable number of internal echoes, localized at the anterior border of the sternocleidomastoid muscle. Therefore, ultrasound permits accurate differentiation between laryngoceles and branchiogenic cysts. Most other lateral cervical masses are discerned by their solid appearance on ultrasound.

Intralaryngeal masses may be neoplasms, internal laryngoceles or laryngeal cysts. Neoplasms appear as solid lesions in our experience. We do not have ultrasound experience with laryngeal cysts. Differentiation from an internal laryngocele on grounds of ultrasound findings alone is probably impossible, since the topographic relation to the ventricle of Morgagni cannot be established at ultrasound.

All laryngoceles appeared to contain mucus, whereas these lesions have always been regarded as air-containing sacs. It can be speculated that there are two different kinds of laryngoceles. Firstly, lesions that are present permanently, and, secondly, laryngoceles which are provoked by increased intralaryngeal pressure. The former lesions are usually characterized by an obstruction at the ventricle of Morgagni. The resulting cavity is lined with mucosa and filled with mucus. In our experience, this is the most common laryngocele.

Celes which are related to intralaryngeal pressure communicate with the air in the larynx and will be filled with air. These lesions were not encountered. Theoretically, such lesions

cannot be assessed by ultrasound. Presumably, CT and conventional tomography are more appropriate in these cases.
The results of conventional tomography were poor. All lesions were depicted by this technique, but were misinterpreted as neoplasms (solid masses).

Both CT and conventional tomography are time-consuming and associated with radiation exposure. Considering the characteristic findings at ultrasound examination and the drawbacks of the other imaging modalities, ultrasound examination may be used as the initial imaging modality for evaluation of an elusive neck mass or when a laryngocele is suspected. When ultrasound examination is inconclusive, CT and/or endoscopy are indispensable.

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Chapter III.4

Comparison of palpation, ultrasound examination and CT in localizing tumors of the parotid gland

Abstract

The objective of this study was to determine the predictive value of palpation, ultrasound examination and CT to localize parotid gland tumors. The results of these diagnostic tests were compared to the operative findings in 35 surgically treated patients. The localization in either the superficial or deep lobe appeared to be best predicted by ultrasound examination. The use of certain anatomic reference points appeared to be of value as far as ultrasound examination and CT were concerned.

Introduction

In the surgical management of parotid gland tumors it is convenient for the surgeon to have knowledge of the exact localization of the lesion. It is very difficult in some cases to determine pre-operatively in which of the two parotid lobes the mass is situated. Little is known of the value of radiologic imaging in this respect. Probably, this is because the facial nerve, which divides the parotid gland, cannot be visualized by any imaging modality. In this study some definitions and certain anatomic reference points were used to predict the course of the facial nerve, and thereby the localization of the lesion.

Patients and methods

Thirty five patients with a mass in the parotid gland were examined preoperatively by physical examination and ultrasound examination. Physical examination was performed by an experienced head and neck surgeon. Ultrasound examinations were performed with 5.0 and 7.5 MHz transducers.

In 27 of the 35 patients CT was performed on clinical grounds. Six mm axial sections parallel to the hard palate were made in case of huge masses. In smaller lesions 3 mm sections were used.

Physical examination, ultrasound examination and CT were performed by independent investigators.

The definitions and reference points which were used during this study are (fig. 1):

- pre-auricular tumors (region I) and masses in the caudate pole (region III) are in the superficial lobe;
- when the retromandibular vein is visualized, its course is used as a partition between the superficial and the deep lobe in region II. When this vein is not visualized, a line drawn in the produced part of the mandible in a transverse section of the parotid gland is taken (fig. 2, 3, 4) and used as the division between the superficial and the deep lobe;

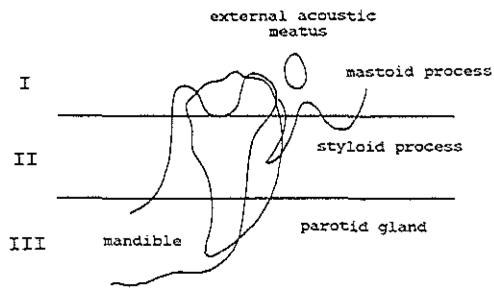

Fig. 1 *Schematic drawing of a lateral view of the region of the parotid gland. The division of the parotid gland into a preauricular part (region I), a middle part (region II) and a caudal part (region III) is shown. The lines used in dividing the parotid gland into 3 regions are drawn at the level of the mastoid process and just above the angle of the mandible.*

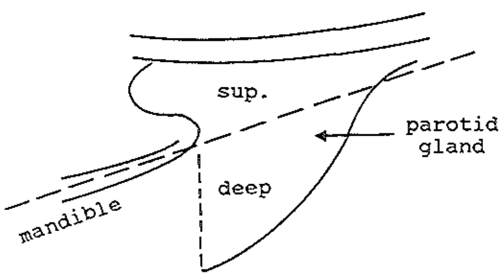

Fig. 2 *Schematic drawing of an ultrasound image representing the subdivision of the parotid gland into a superficial and a deep lobe (transverse section in region II).*

- in case of large tumors which comprise almost the entire gland, the thickness of the remaining normal glandular tissue is used as a criterion: when more normal glandular tissue is found lateral to the tumor than medial, the tumor is considered to be originating in the deep lobe (fig. 5). Conversely, the tumor is considered to be situated in the superficial lobe, when more normal tissue is found medial to the mass.

The results of palpation, ultrasound and CT were compared with the operative findings.

Results

The results are presented in Table 1.

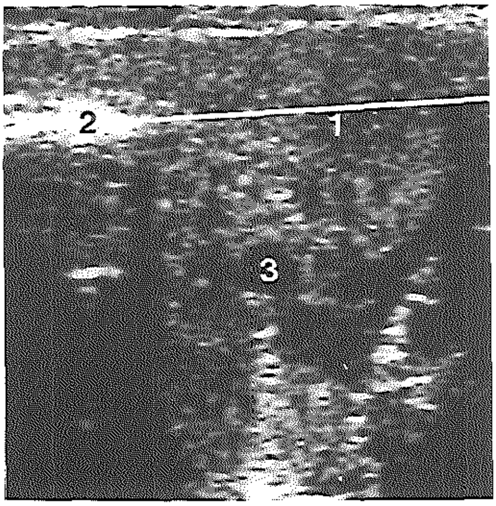

Fig. 3 *Transverse ultrasound section of the parotid gland in region II according to fig. 2. The relationship of the parotid gland to the mandible is estimated. The retromandibular vein is shown.*
1 parotid gland
2 mandible
3 retromandibular vein

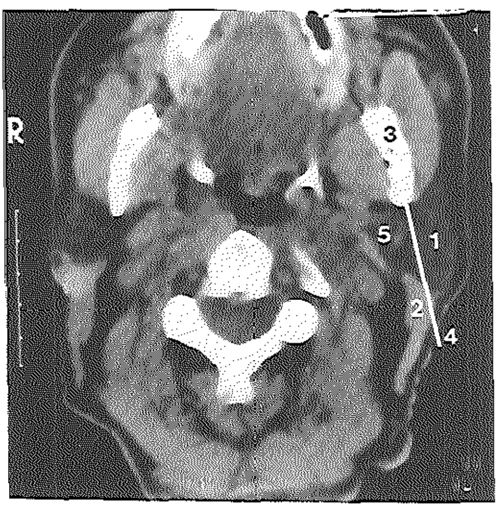

Fig. 4 *Transverse CT section at the level of the parotid gland in region II.*
Schematic divison of the parotid gland into a deep and superficial part by a line in the produced part of the mandible.
1 parotid gland
2 sternocleidomastoid muscle
3 mandible
4 line dividing the parotid gland into a superficial and a deep part
5 vascular structures in the parotid gland

Peroperative findings

In 25 out of 35 patients the masses appeared to be localized in the superficial lobe; in 7 patients in the deep lobe. The lesions in the remaining 3 patients were localized in both the superficial and the deep lobe. In 31 patients a single mass was found. In 4 patients multiple masses were present: two of them only in the superficial lobe; in the other 2 patients they were localized throughout the entire gland.

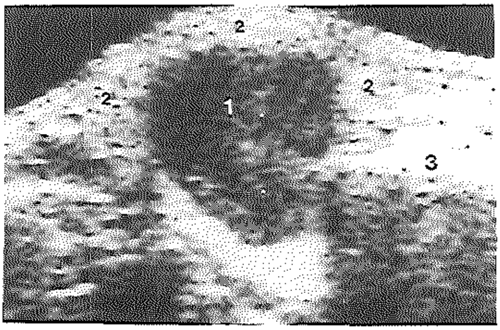

Fig. 5 *Transverse section of the parotid gland in region II. A large pleiomorphic adenoma, presenting as a low echogenic, well-defined mass with posterior acoustic enhancement is located adjacent to the mandible. The layer of normal parenchymal tissue superficial to the tumor suggests a localization in the deep lobe.*
1 pleiomorphic adenoma
2 normal parenchyma of the parotid gland
3 reflection of the mandible

Palpation

Preoperative palpation resulted in a correct prediction of localization in 13 of 35 patients; these 13 masses were all in the superficial lobe. In 12 of these 13 patients the lesions were localized in region I or III (fig. 1). In 20 cases no localization could be established. In 2 cases the localization appeared to be incorrect: in one patient a mass in the superficial lobe was thought to be outside the parotid gland; in another patient, a deep lobe tumor was assumed to be part of the superficial lobe.

Ultrasound examination

In 31 of 35 patients the localization was correctly made by ultrasound.
In one patient with a pleiomorphic adenoma in the superficial lobe, posterior acoustic enhancement caused an under-estimation of the volume of the remaining normal tissue. Consequently, the superficial lobe tumor was considered to be part of the deep lobe.
In 3 patients ultrasound examination was inconclusive because the above mentioned definitions did not apply. In these patients the lesions were in region II, at the level of the mandible. The amount of normal parenchymal tissue superficial to the tumor was equal to the amount of parenchyma medial to it. Furthermore, the retromandibular vein was not visualized in these cases. Therefore, none of the criteria mentioned in the patients and methods section could be used.

Table 1 Results of palpation, ultrasound examination (US) and CT regarding the localization of parotid gland tumors. The results are correlated with the operative findings of 35 patients.

	OPERATIVE FINDINGS Superficial	Deep	S/D
PALPATION n=35			
Superficial	13	1	0
Deep	0	0	0
Superficial/deep	0	0	0
Inconclusive	11	6	3
-	1	0	0
Not performed	0	0	0
ULTRASOUND n=35			
Superficial	21	0	0
Deep	1	7	0
Superficial/deep	0	0	3
Inconclusive	3	0	0
-	0	0	0
Not performed	0	0	0
CT n=27			
Superficial	13	1	0
Deep	0	2	0
Superficial/deep	0	0	2
Inconclusive	4	1	0
-	3	1	0
Not performed	5	2	1

S/D = superficial and deep
\- = no tumor visualized (CT, US) or interpreted as extraglandular (palpation)

CT

The correct localization was predicted in 17 of 27 patients by CT. In 5 cases CT was inconclusive. In one patient a deep lobe mass was predicted to be in the superficial lobe. Another mass was not depicted due to artefacts. In 3 cases the parotid gland appeared inhomogeneous and slightly enlarged, but no tumor could be delineated.

Discussion

In general, it is difficult to establish the exact localization of a parotid tumor by palpation. Regarding radiodiagnostic feasibilities, Whyte[1] studied the value of ultrasound examination

and CT in the localization of parotid gland tumors in 18 patients. High accuracy-rates of both methods were reported.
In our experience, radiologic imaging is indeed superior to clinical examination. However, a 100% accuracy could not be achieved. This is due to the fact that the facial nerve itself is not visualized. Its course has to be judged by anatomic references, and as a consequence of the latero-caudal course of the facial nerve, different references have to be employed (fig. 1, 2). While using different anatomic references at different levels in the parotid, it is clear that this method is of limited value in large tumors since these tumors present themselves at different levels. This is the reason for other criteria for large tumors in this study.
Applying the criteria which were mentioned earlier, ultrasound examination proved to be the most reliable method: accuracy was 89%, whereas the accuracy-rates of CT and palpation were 63% and 37% respectively.
Palpation correctly localized superficial masses in the parotid gland in regions I and III only. In deep lobe tumors and tumors in region II palpation was inconclusive.
The low accuracy of CT is caused by the fact that 4 masses were not depicted. Failure of CT to localize the tumor in the cases where the tumor was depicted, is caused by poor visualization of the retromandibular vein in the absence of fat. Furthermore the axial scanning direction in routine CT is not favourable in defining the caudate pole, and coronal scanning may be necessary for additional information.
No method of investigation was able to detect the small extension into the deep lobe of 3 tumors located in the superficial lobe, as established during surgery.
In general, parotid gland tumors produce posterior acoustic enhancement at ultrasound examination. As a result, the amount of tissue medial to the mass may be difficult to judge, and an under-estimation of the remaining normal tissue may occur. This was indeed the case in the failure of ultrasound in this study. Knowledge of this pitfall and using different scanning directions during ultrasound examination may reduce ultrasound failures.

Conclusions

1 Ultrasound examination was found to be superior to palpation and CT in predicting the exact localization of tumors in the parotid gland.
2 Palpation was reliable in tumors of the pre-auricular region and caudate pole.

Reference

1. Whyte A.M. and Byrne J.V. A comparison of computed tomography and ultrasound in the assessment of parotid masses. Clin. Radiol. 1987; 38: 339-343

Chapter III.5

Evaluation of tumors of the parotid gland by ultrasound examination

Abstract

This study was focused on the possibilities of ultrasound examination to differentiate between benign and malignant parotid gland tumors. In addition, the ultrasound patterns of the most common histological parotid tumor types were assessed. Finally, the value of cytologic examination of parotid gland lesions was judged.

Ultrasound examination provided correct information regarding boundaries and delineation of the tumor in all patients. Reliable differentiation between benign and malignant tumors on grounds of ultrasound characteristics turned out to be impossible. Some tumors (e.g. pleiomorphic adenoma and Whartin's tumor) showed a relatively constant ultrasound pattern. However, for a reliable preoperative diagnosis, additional investigation by means of cytologic examination is recommended.

Introduction

Ultrasound has become an important diagnostic imaging modality in the head and neck region since the development of high-frequency, high-resolution transducers. Because of its superficial position the parotid gland is easily accessible for examination by ultrasound. Several authors[1 2 3 4 5 6 7 8] have reported the value of ultrasound in salivary gland disease. However, these studies are not unequivocal in determining the value of ultrasound examination in differentiation between benign and malignant tumors of the parotid gland. In this report the ultrasonic patterns of 41 tumors of the parotid gland will be presented. Preoperative sonographic findings are compared to the results of histopathologic examination of the resected specimens. The place of ultrasound in analyzing tumors in the parotid area will be discussed.

Patients and methods

Forty patients (17 males and 23 females) aged 28-72 years (mean age 56 years) with a mass in the parotid gland were examined by ultrasound prior to surgery.

All patients were examined in supine position in longitudinal, transverse and oblique directions. The margins, configuration and aspect of 41 tumors were evaluated.

In 31 patients (32 tumors) a fine needle aspiration biopsy was performed on clinical grounds. The smears were judged by an experienced cytopathologist. The results of the ultrasound and cytologic examinations were compared with the operative findings and histopathologic findings of the surgical specimen. The histopathologic specimens were reviewed by the head of the department of Histopathology (R.O. van der Heul, M.D., Ph.D).

Results

Forty patients underwent surgery for 41 tumors of the parotid gland. Histopathologic examination demonstrated 30 benign lesions and 11 malignancies (9 primary malignancies, 2 metastases). The tumors varied in size from 0.5 to 5.0 cm with a mean of 2.7 cm in benign tumors and 1.7 cm in malignant tumors. Seven malignant lesions were less than 1.5 cm. The histologic diagnoses and the ultrasonic characteristics of the tumors are presented in Table 1. All tumors, including one cyst, appeared solid on ultrasound examination (fig. 1).

Most pleiomorphic and monomorphic adenomas appeared as homogeneous, lobulated, well-defined and solid tumors (fig. 2). In 7 of 25 tumors however, an inhomogeneous aspect was observed (fig. 3).

Whartin's tumors (cystadenolymphoma's) appeared as solid tumors of low echogenicity, frequently with cystic areas (fig. 4).

Many malignant tumors had an inhomogeneous aspect but 5 of 11 lesions (45%) showed a regular parenchymal pattern. In contrast to what is generally stated, 9 of 11 malignant (82%) tumors showed well-defined margins (fig. 5, 6, 7). In the remaining 2 malignant lesions unsharp borders were depicted (fig. 8).

Posterior acoustic enhancement was observed in 25 of 30 benign and in 8 of 11 malignant tumors.

Table 1 Ultrasound characteristics of 41 parotid gland tumors.

	HISTOPATHOLOGY					
	PLEIO	MONO	WHARTIN	METAST	MAL	CYST
n	23	2	4	2	9	1
HOM	16	2	3	2	3	1
INHOM	7	0	1	0	6	0
SHARP	20	2	3	1	8	1
UNSHARP	3	0	1	1	1	0
CYSTIC	3	0	2	0	1	0
PAE	19	2	3	1	7	1
LOB	16	1	1	0	4	0

n = number of tumors
PLEIO = pleiomorphic adenoma
MONO = monomorphic adenoma
WHARTIN = Whartin's tumor
METAST = metastasis
MAL = malignancy
CYST = epidermal cyst
HOM = homogeneous
INHOM = inhomogeneous
SHARP = sharp borders
UNSHARP = unsharp borders
CYSTIC = cystic components
PAE = posterior acoustic enhancement
LOB = lobulated aspect

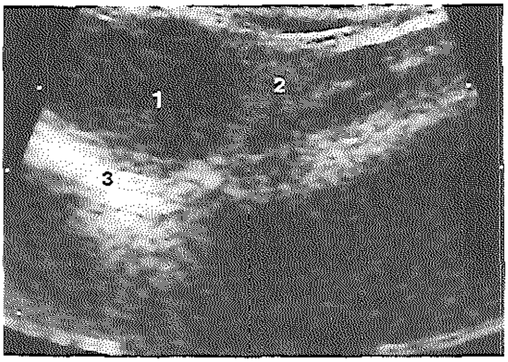

Fig. 1 *Longitudinal section of the parotid gland. The epidermal cyst shows multiple echo reflections inside, simulating a solid tumor.*
1 epidermal cyst in the superficial part of the parotid gland
2 normal parenchyma of the parotid gland
3 posterior acoustic enhancement

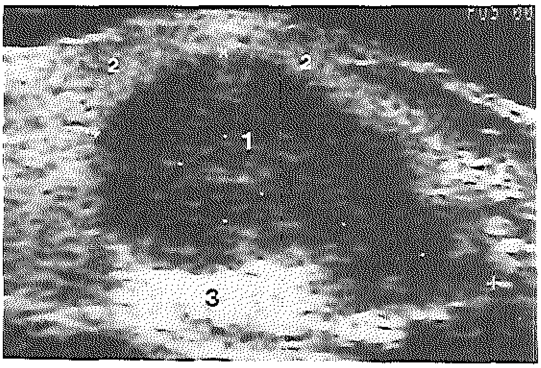

Fig. 2 *Longitudinal view of a characteristic pleiomorphic adenoma in the deep part of the parotid gland showing lobulation, well-defined margins, homogeneous pattern and posterior acoustic enhancement.*
1 pleiomorphic adenoma
2 normal parenchyma of the parotid gland
3 posterior acoustic enhancement

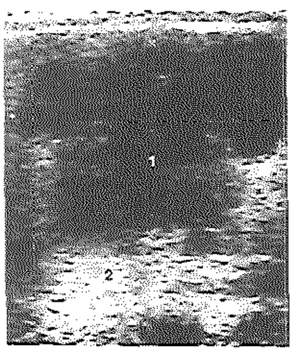

Fig. 3 *Pleiomorphic adenoma in the superficial and deep part of the parotid gland with unsharp borders and an inhomogeneous structure.*
1 pleiomorphic adenoma
2 posterior acoustic enhancement

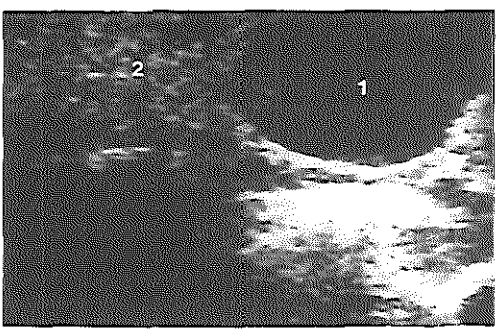

Fig. 4 *Longitudinal section of the parotid gland showing a low echogenic tumor, almost cystic in nature, in the caudate pole on basis of a Whartin's tumor.*
1 Whartin's tumor
2 normal parenchyma of the parotid gland

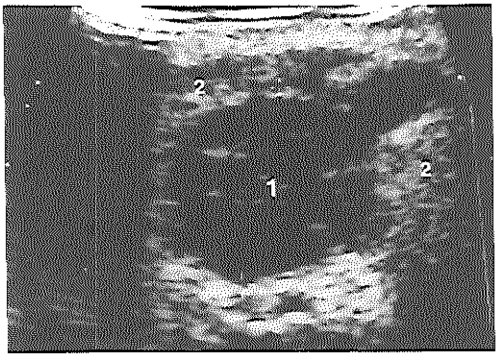

Fig. 5 *Squamous cell carcinoma of the parotid gland with an inhomogeneous structure, but well-defined margins.*
1 carcinoma
2 normal parenchyma

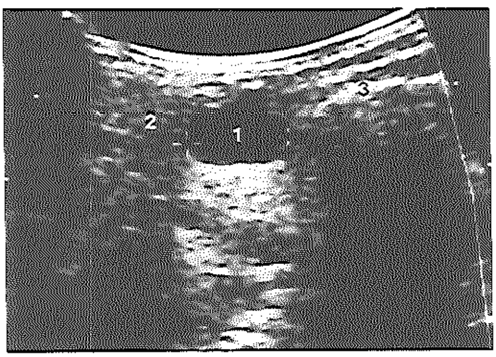

Fig. 6 *Transverse section of the parotid gland. Small, lobulated, homogeneous, well-defined, low echogenic mass in the superficial lobe of the parotid gland. Histopathologic examination revealed an acinic cell tumor.*
1 acinic cell tumor
2 normal parenchyma
3 mandible

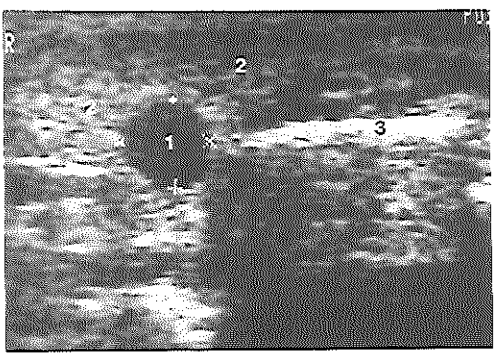

Fig. 7 *Transverse view of an acinic cell tumor showing well-defined margins and a homogeneous structure.*
1 acinic cell tumor
2 normal parenchyma
3 mandible

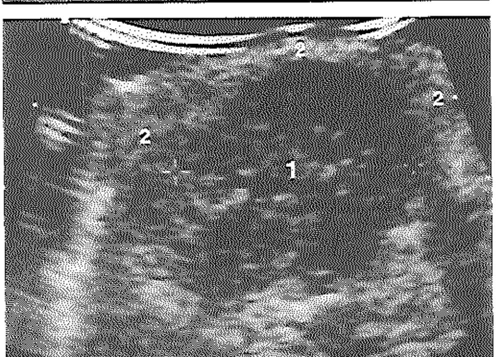

Fig. 8 *Adenocarcinoma in both superficial and deep lobe of the parotid gland. The tumor is marked by inhomogeneity and for the most part unsharp borders.*
1 adenocarcinoma
2 normal parenchyma

The frequency of characteristics in benign and malignant tumors is shown in Table 1.
In 32 cases cytologic examination was used for differentiation between benign and malignant disease. The results of the cytologic examination are presented in Table 2. In 29 cases (91%) a correct cytologic diagnosis was achieved, there were no false positive or false negative results. Three aspirations (9%) did not allow diagnosis because the smears did not contain representative cells (Pap 0).

Table 2 The results of cytologic examination with regard to the differentiation between benign and malignant lesions in 32 parotid gland tumors.

CYTOLOGY	HISTOPATHOLOGY BENIGN	HISTOPATHOLOGY MALIGNANT
BENIGN	20	-
MALIGNANT	-	9
INCONCLUSIVE	3	-

In one case a cystadenopapillary carcinoma at cytology was shown to be an acinic cell tumor at histopathologic examination (Table 3). The remaining cytologic diagnoses were in accordance with the findings at histopathologic examination.

Discussion

In previous reports several authors described a positive contribution of ultrasound to differentiate between benign and malignant tumors of the parotid gland[1 2 3 4 5]. The number of patients in these studies varied between 13 and 141 patients, the accuracy rates ranged from 75% to 85%. In contrast, several authors[6 7 8] concluded that differentiation between benign and malignant lesions was not possible on grounds of ultrasound examination.
The criteria, advocated in literature[1 2 3 4 5], used to discern benign and malignant disease are the homogeneity of the parenchymal tissue and the demarcation of the borders of the lesion. A benign solid lesion is generally assumed to be characterized by a homogeneous parenchymal texture and well-defined margins, whereas a malignant lesion is supposed to be inhomogeneous with ill-defined borders. In our study the aspect of many tumors did not comply with these clear characteristics of benign and malignant lesions. Many malignancies showed well-defined margins, whereas several pleiomorphic adenomas appeared to have an irregular parenchymal texture. This may be caused by very small cystic components and a variety of other contents: an epithelial component mixed with mucoid, myxomatous, fibrous and chondroid areas.
Most neoplasms had a low echogenic appearance, with posterior acoustic enhancement as a result of the surrounding homogeneous and highly echogenic tissue of the normal

Table 3 The results of cytologic examination in 32 tumors of the parotid gland compared to the histopathologic findings.

n	HISTOPATHOLOGY	CYTOLOGY
16	pleio	pleio
3	Whartin	Whartin
1	cyst	cyst
1	adenoca	adenoca
1	adenoca	Pap. V
1	sq.ca	sq.ca
1	sq.ca	Pap. IV
2	ac.cell	ac.cell
1	ac.cell	cystadeno
1	sarc	Pap. IV, mesenchymal
1	undiff.ca	Pap. V
2	pleio	inconclusive
1	mono	inconclusive

n = number of tumors
pleio = pleiomorphic adenoma
mono = monomorphic adenoma
Whartin = Whartin's tumor
adenoca = adenocarcinoma
sq.ca = squamous cell carcinoma
ac.cell = acinic cell tumor
cystadeno = cystadenopapillary carcinoma
sarc = leiomyosarcoma
undiff.ca = undifferentiated carcinoma

parenchyma.
In general, simple cysts do not present as entirely echo free structures. Because of the mucinous contents, a cyst often shows internal reflections and may be mistaken for a solid lesion, as was the case with the cyst in our study.
In literature[1,2,3,4,5], a homogeneous parenchymal pattern and well-defined borders are said to be characteristic features of benign parotid tumors. Approximately 80% of the benign tumors in these studies fulfilled these criteria for benign disease. When used in our patients similar results are obtained (Table 4). However, considering the fact that 80% of the parotid gland tumors are benign, the predictive value of homogeneity and sharp demarcation is not very impressive. Other combinations of criteria are even less reliable (Table 4).
Therefore accurate and reliable ultrasound definitions for tissue diagnosis cannot be established and further differentiation by fine needle aspiration biopsy, either conventional or performed under ultrasound guidance, is necessary. The findings of ultrasound in combination with the results of cytologic examination allowed correct differentiation in benign and malignant tumors in 29 of 32 cases (90.6%). The accuracy rates which are mentioned in the literature are even slightly better (95% or more) as recorded in a review of the literature by Layfield et al.[9] Therefore, cytologic examination can provide a preoperative accurate

Table 4 Several combinations of ultrasound criteria to discern benign and malignant disease. When these combinations are compared to the histopathological diagnosis, it appears that these criteria are not useful.

ULTRASOUND	HISTOPATHOLOGY BENIGN	HISTOPATHOLOGY MALIGNANT
HOMOGENEOUS + SHARP	22	4
INHOMOGENEOUS + UNSHARP	2	2
INHOMOGENEOUS + SHARP	5	4
HOMOGENEOUS + UNSHARP	1	1

assessment as to whether the lesion is benign or malignant making it possible to plan with the patient the type of treatment necessary, including the possibility of having to resect the facial nerve in malignant disease. It also allows for preoperative planning of possible interstitial radiation to the tumor bed at the end of the procedure, rather than the usual difficulties of not knowing whether this might be necessary until the results of frozen section diagnosis at the time of surgery are available.

It is known from the series of Qizilbash[10], who studied the accuracy of fine needle aspiration of salivary glands, that nearly two thirds of their benign group of salivary gland lesions were not tumors. It can be speculated that when ultrasound would have been used, the depiction of a normal but enlarged gland, might have prevented a cytological examination in some of these patients. Cytologic examination in these cases usually does not provide useful information, and may be confusing instead: if smears show normal epithelial cells in a patient who is expected to have a tumor, most surgeons will perform an excision of the gland. Ultrasound examination may prevent such an unnecessary exploration.

In case of a malignant parotid lesion, the ultrasound examination should include the entire neck to detect nodal metastases (part II).

Finally, since ultrasound can detect small parotid gland lesions it can be used to detect contralateral lesions (e.g. in Whartin's tumor). Furthermore, ultrasound may exclude parotid gland tumors in cases of facial nerve paralysis.

Conclusions

1 Ultrasound can identify and delineate parotid gland tumors.
2 For differentiation between benign and malignant disease, ultrasound is not appropiate.
3 In the diagnosis of parotid gland tumors, cytologic examination is useful and accurate.

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Chapter III.6

Ultrasound examination in non-neoplastic disease of the salivary glands

Abstract

The diagnostic significance of ultrasound examination in non-neoplastic disease of the salivary glands was investigated in 36 patients. The ultrasonic patterns in acute, suppurative and chronic inflammation, calculi and dilatation of ducts were correlated with clinical examination, sialography and/or histopathologic examination.

The ultrasound findings in acute inflammation, with or without abscess-formation, and sialolithiasis appeared to be quite specific. The contribution of ultrasound examination in chronic disease was not conclusive. The place of ultrasound examination in the diagnostic work-up of inflammatory disease was defined.

Introduction

History taking and physical examination may lead to the correct diagnosis of inflammatory salivary gland disease in a high number of cases. However, differentiation from lymphadenopathy or neoplasms is sometimes difficult. Furthermore, in clinically clear-cut cases of sialo-adenitis it is often impossible to exclude sialo-lithiasis or suppuration. Sialography may be useful, but is contraindicated in acute inflammation, and sometimes the duct cannot be cannulated.

The superficial location of the salivary glands makes these structures accessible for high resolution ultrasonography. Several reports have been published on the value of ultrasound examination to assess tumefaction in the salivary glands, mainly the parotid gland (chapter III.5). However, the role of ultrasound examination in inflammatory disease of the salivary glands has received less attention in literature.

In this study the aspect of normal glandular tissue and the changes in inflammatory disease are described. Visualization of salivary stones and ductal pathology is discussed.

Patients and methods

Thirty-six patients with clinical evidence of inflammatory disease of the salivary glands were examined by ultrasound examination. In 16 patients (21 glands) with chronic sialo-adenitis and/or suspection of sialo-lithiasis, sialography was performed. Sialography was used to verify the ultrasound findings with respect to ductal dilatation. The encouraging results of ultrasound in the detection of parenchymal changes and salivary stones, were later reason to leave out sialography as a routine.

Because surgery is indicated in just a minor number of patients with inflammatory disease of the salivary glands, the final diagnosis was established at histopathologic examination of the resected specimens in only 9 patients. In the remaining 27 patients the diagnosis was made on grounds of the clinical course.

Results

The parotid and submandibular glands were involved in 15 and 21 patients respectively. The distribution of pathology is presented in Table 1.

Table 1 Distribution of inflammatory disease in this study.

	PAROTID GLAND	SUBMANDIBULAR GLAND
SIALO-ADENOSIS	1	2
SIALO-ADENITIS	10	6
SIALO-LITHIASIS	1	3
SIALO-ADENITIS + SIALO-LITHIASIS	3	10

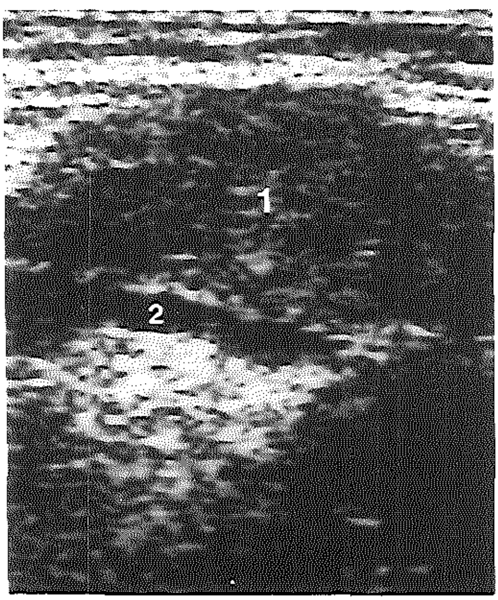

Fig. 1 *Section parallel to the mandible. Chronic sialo-adenitis of the submandibular gland, marked by inhomogeneity of the parenchymal pattern, low echogenicity and rounding of the margins.*
1 submandibular gland
2 digastric muscle

Parenchymal texture in case of clinical evidence of inflammation

In 26 of 36 patients pathologic changes of the normal homogeneous, highly echogenic parenchymal pattern were found by ultrasound examination. In acute sialo-adenitis a low echogenic aspect of the parenchyma was observed. These changes were limited to one or more areas or were uniformly distributed throughout an enlarged gland. In chronic sialo-adenitis a low echogenic appearance with inhomogeneity of the parenchyma, probably

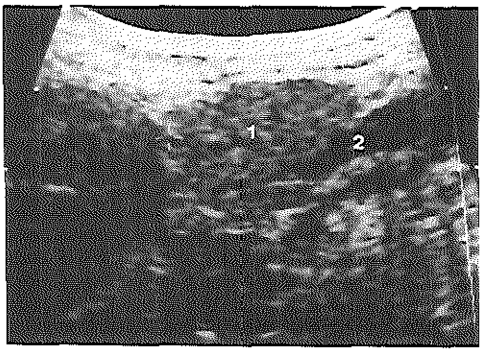

Fig. 2a *Section parallel to the mandible. Chronic sialo-adenitis of the submandibular gland. Atrophy of the gland and rounding of the margins are clearly demonstrated.*
1 submandibular gland
2 mylohyoid muscle

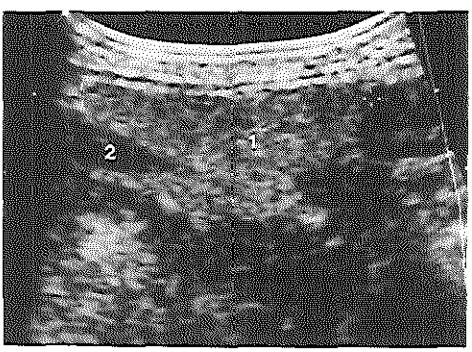

Fig. 2b *Section parallel to the mandible. The contralateral, normal, submandibular gland in the same patient.*
1 submandibular gland
2 mylohyoid muscle

caused by fibrosis, was observed (fig. 1). In clinically distinct cases of chronic sialo-adenitis the increment of fibrosis led to a high echogenic parenchymal texture, more demarcated and rounded margins and atrophy of the gland (fig. 2a and 2b). In 2 patients ultrasound examination revealed small cysts filled with echogenic material due to suppuration (fig. 3a and 3b). In 1 patient swelling of the submandibular region was caused by a large infiltrate surrounding the inflamed submandibular gland. Small accompanying lymph nodes were demonstrated by ultrasound examination, suppuration was excluded.

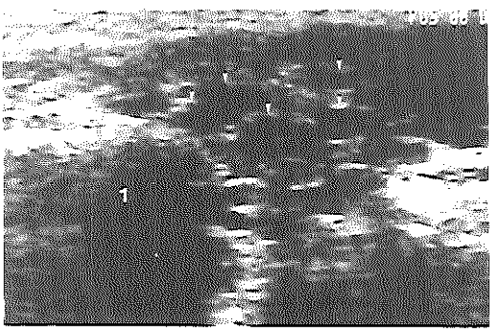

Fig. 3a *Transverse view of the parotid gland at the level of the ramus of the mandible. Cystic dilatations of the ductal system are presented as low echogenic structures (arrows) throughout the gland in this case of chronic sialo-adenitis.*
1 acoustic shadowing of the mandible

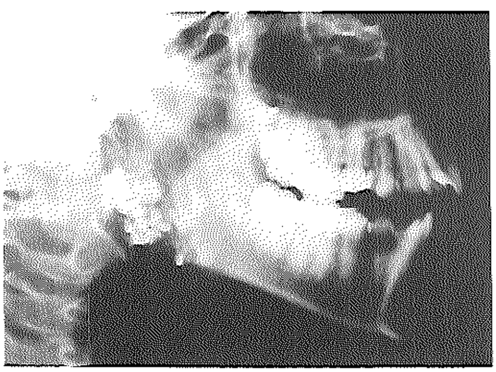

Fig. 3b *Lateral X-ray view of the parotid region. Sialographic examination in the same patient as fig. 3a. The cystic dilatations of the ductal system are filled with contrast medium.*

In 9 patients a normal parenchymal pattern was observed. In 4 of these patients ultrasound examination revealed an enlargement of the gland (2 sialo-adenosis, 2 sialo-lithiasis). The glands in the remaining 5 patients had a normal size (1 sialo-lithiasis, 1 sialo-adenitis, 3 sialo-lithiasis with sialo-adenitis).
In one patient ultrasound examination was performed after excision of the submandibular gland. This patient had persisting complaints. Ultrasound examination revealed a cavity with 2 stones in the submandibular region.

Salivary stones

Sialo-lithiasis was established in 17 patients.
In 10 patients the diagnosis sialo-lithiasis was verified at surgery or by a spontaneous release of the stone. In 9 of these patients the stone was detected at ultrasound examination (fig. 4). In another 7 patients ultrasound revealed calculi. In 4 of these 7 patients the ultrasound findings were confirmed by plain radiography and/or sialography. In one patient no additional investigations were performed. In the remaining 2 patients plain radiography and/or sialography were negative. However, the ultrasound findings were identical to the verified cases. At ultrasound examination the calculi presents as a strong reflection with posterior acoustic shadowing. This highly characteristic pattern is validated in other studies[2,3,5].

Ductal morphology

In 21 glands (16 patients) sialography was performed, including 5 failures to perform sialography.
The investigation of the remaining 16 glands revealed 7 glands
with dilated ducts. Ultrasound examination was able to detect these dilatations in all 7 cases (fig. 5 and 6). The results are presented in Table 2.

Table 2 Visualization of ductal dilatation at ultrasound examination of 16 glands in which sialography was performed.

ULTRASOUND	SIALOGRAPHY +	SIALOGRAPHY –
+	7	0
–	0	9

\+ = ductal dilatation
\- = absence of ductal dilatation

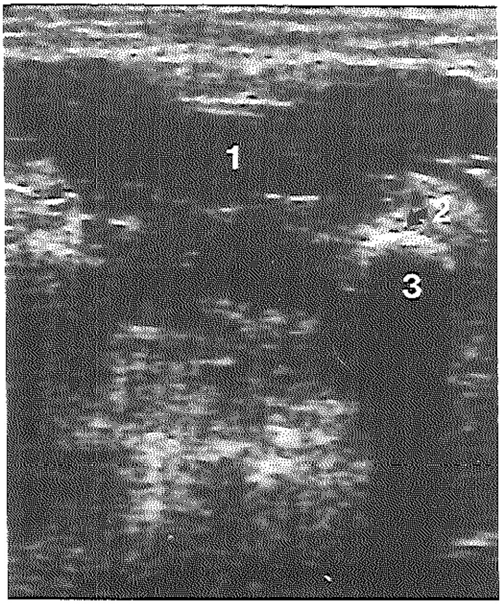

Fig. 4a *Transverse sonographic section in the midline of the floor of the mouth. A stone in the submandibular duct is visualized as a strong reflection with an acoustic shadowing.*
1 musculature of the floor of the mouth
2 reflection of the stone
3 acoustic shadowing of the stone

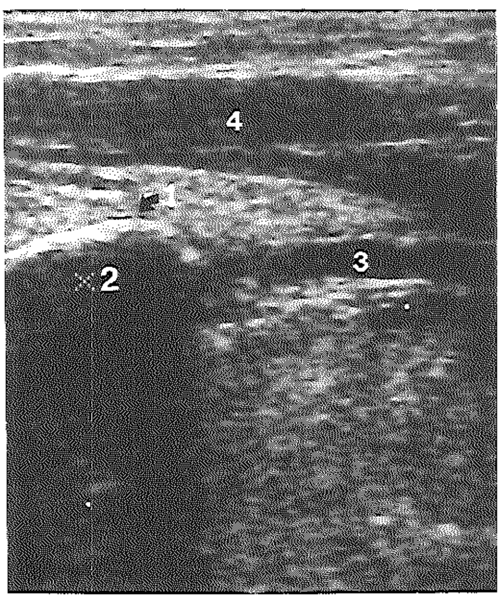

Fig. 4b *Longitudinal section, parallel to the mandible, showing a stone distal to the submandibular duct, which is markedly dilated proximal to the stone.*
1 reflection of the stone
2 acoustic shadowing caused by the stone
3 dilated submandibular duct
4 muscles of the floor of the mouth

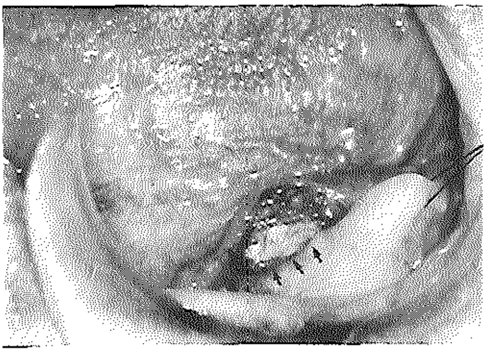

Fig. 4c *View of the floor of the mouth after incision of the submandibular duct. A large stone is shown (arrows).*

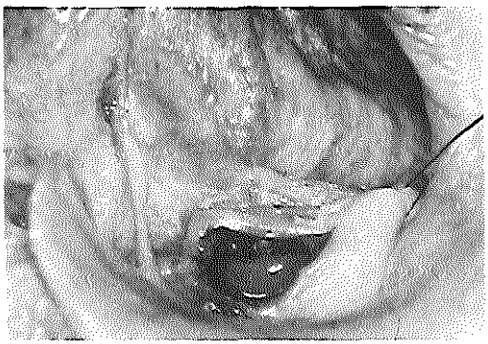

Fig. 4d *View of the floor of the mouth after removal of the stone.*

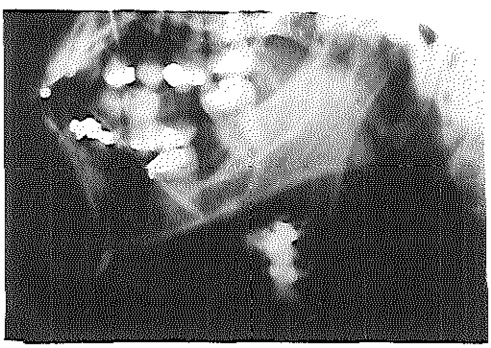

Fig. 5a *Lateral X-ray view of the submandibular region. Sialographic examination demonstrates marked dilatation of the submandibular duct.*

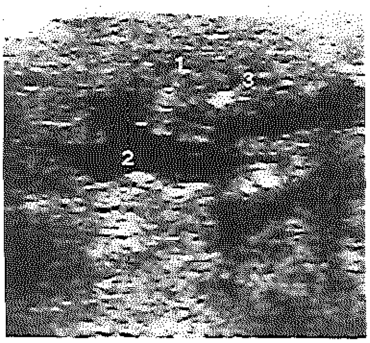

Fig. 5b *Ultrasound examination of the same patient. Section parallel to the mandible. The dilated submandibular duct is seen as a wide echo free/low echogenic tubular structure. The intraglandular branches are not dilated.*

1 submandibular gland
2 dilated submandibular duct
3 reflection of a small parenchymal stone

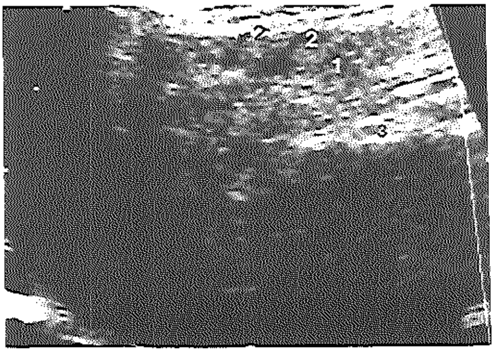

Fig. 6a *Transverse view of the parotid gland, which reveals an inhomogenic pattern of the parenchyma on the basis of small low echogenic areas representing small cystic dilatations of the ductal system.*
1 parotid gland
2 cystic dilatations
3 mandible

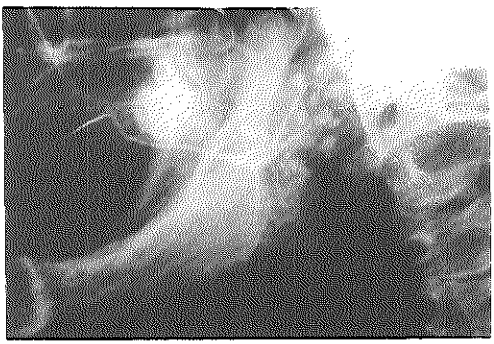

Fig. 6b *Lateral X-ray view during sialographic examination of the same patient as in Fig. 6a. Small, cystic dilatations of the ductal system are filled with contrast. The main duct is not dilated.*

Discussion

The ultrasound characteristics of normal glandular tissue are homogeneity and a rather high echogenic pattern of the parenchyma. A variety of changes can be seen in sialo-adenitis, mostly depending on the duration of the inflammation. A normal ultrasound pattern of the parenchyma can be seen in patients with sialo-adenitis with a relatively short history of disease, in the course of which apparently no changes of the parenchymal pattern have occurred. The changes in acute sialo-adenitis may be confined to an enlargement of the gland. However, in most cases inflammation is expressed by a decrease of the echogenicity of the parenchyma which can be focal or uniformly distributed throughout the gland. Accompanying enlargement of lymph nodes can occur. In case of parotitis these may be found to be intraglandular.
Inhomogeneity and an increase in echogenicity in sialo-adenitis are features of longstanding disease caused by fibrosis. The increasing fibrosis leads to atrophy of the gland and rounding of the margins in advanced cases.

A major advantage of ultrasound over sialography is that it can be performed in cases of acute sialo-adenitis.
Another useful property of ultrasound examination is its sensitivity and specificity for abscess formation[1]. Although Diederich and Schadel claim sensitivity and specificity to be as

high as 100%[2,3], in our experience suppuration is not always that evident. Frequently, abscesses are surrounded by a thick, irregular wall. The ultrasound appearance of an abscess can vary from low to high echogenicity, depending on the constitution of the contents. An abscess with a thick debris will have a more echogenic appearance, while abscesses with relatively clear contents appear as low echogenic. Ultrasound guided aspiration can help to differentiate in these cases. The aspirate can be used for culture, gram stain and/or cytologic examination. In addition, accurate localization of abscesses for incision and ultrasound guided percutaneous drainage may be established by ultrasound examination (part IV).
Sialo-adenitis is frequently associated with the formation of calculi. The detection and the estimation of the precise localization of calculi is important in the management of sialo-lithiasis. In case of a ductal stone, an incision of the duct may suffice to remove the stone. However, in case of parenchymal stones excision of the gland has to be considered. In this study ultrasound examination proved to be a reliable method to detect ductal and/or intraglandular stones. This is supported by other studies[2,3,4]. Calculi may be recognized as a bright reflection with posterior acoustic shadowing. The sensitivity for the detection of calculi is reported to vary between 71.4%[2] and 100%[3]. In our study the sensitivity was 94%. Only the submental region immediate behind the mandible cannot be investigated properly by ultrasound due to the strong reflection and posterior acoustic shadowing of the mandible. However, calculi in the main duct always cause dilatation of the intra- or extraglandular ducts. This dilatation of ducts is clearly visible with ultrasound examination[1,2,4,5] and may suggest obstruction. Therefore, when ultrasound examination shows dilatation of the submandibular ducts, but a calculus is not depicted, clinical examination or a spot film of the floor of the mouth may reveal pre-papillary stones. There are no limitations in the ultrasound examination of the main parotid duct. As a result of the course of the duct superficial to the masseteric muscle and the mandible, the pre-papillary region is well assessed at ultrasound examination.

Conclusions

1 Acute sialo-adenitis is characterized by low-echogenic, ill-defined areas, focal or uniform distributed throughout the gland, which may be enlarged.
2 Chronic sialo-adenitis leads to an inhomogeneous parenchymal pattern as a result of the increase of fibrosis. In advanced cases the echogenicity is increased and atrophy of the gland occurs with rounding of the margins.
3 Suppuration may be clear at ultrasound examination, but sometimes confirmation by ultrasound guided fine needle aspiration is needed.
4 The ultrasound features of calculous structures result in a reliable demonstration of salivary stones.
5 Dilatation of ducts is visualized with a high reliability at ultrasound examination.

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Chapter III.7

Ultrasound examination in the diagnosis of cervical tuberculous adenitis

Abstract

Ultrasound examination of cervical tuberculous adenitis (CTA) was demonstrated to produce a characteristic pattern of the affected nodes in the majority of the patients in this study. The contribution of ultrasound examination to the diagnosis and assessment of CTA is evaluated. It is concluded that, since the other diagnostic tests for CTA are not reliable and/or time-consuming, the demonstration of nodal calcifications, conglomerate nodal masses and spread into the subcutaneous tissues at ultrasound examination in patients with elusive cervical masses may result in earlier recognition of CTA.

Introduction

Cervical tuberculous adenitis (CTA) is relatively uncommon in the Western world and the diagnostic modalities available to confirm the diagnosis are not uniformly reliable[1 2 3 4 5]. These factors may result in delay in diagnosis and treatment.

Ultrasound examination of patients with CTA appeared to produce a characteristic pattern in the majority of our patients.

The objective of this study was to determine the possible role of ultrasound examination in earlier recognition of CTA.

Patients and methods

Between December 1984 and December 1988, 20 patients with CTA were seen in the University Hospital Rotterdam. The diagnosis was by ENT- and physical examination, PPD skin-tests, chest X-rays, acid-fast staining, cultures and histopathologic examination. When one or more of the latter four tests were positive, a diagnosis of CTA was established.

In 12 of 20 patients an ultrasound examination of the neck was performed. These 12 patients are the subject of this study.

Retrospectively, records, reports of the ultrasound examination and sonograms were reviewed.

Results

Clinical data and the results of relevant diagnostic tests of 12 patients with CTA are presented in Table 1 and 2.

The age distribution ranged from 5 to 75 years. The male-female ratio was 1:1. Most patients had minimal constitutional complaints and presented because of palpable neck masses. In 3

Table 1 Clinical data and results of relevant diagnostic tests of 12 patients with CTA.

	PATIENT	X-RAY	PPD-TEST	ACID-FAST	CULTURES	ULTRASOUND	CYTOLOGY	HISTOPATHOLOGY	CONCLUSION
1	♀,23 yr	neg	M.Kans. M.Scrof.	neg	neg	pos	–	pos	M.Kans. + M.Scrof.
2	♀,75 yr	pos	neg	neg	M.Tuber.	pos	–	pos	M.Tuber.
3	♀,50 yr	neg	M.Tuber.	neg	M.Tuber.	pos	pos	–	M.Tuber.
4	♂,50 yr	neg	neg	neg	M.Tuber.	pos	–	pos	M.Tuber.
5	♀,40 yr	neg	M.Tuber.	pos	M.Tuber.	neg	–	–	M.Tuber.
6	♀, 7 yr	neg	M.Avium. M.Scrof.	neg	neg	pos	–	pos	M.Avium + M.Scrof.
7	♂, 5 yr	neg	M.Avium	pos	neg	pos	–	pos	M.Avium
8	♀,53 yr	pos	–	neg	neg	pos	pos	–	CTA
9	♂,19 yr	neg	M.Avium	pos	M.Avium	pos	neg	neg	M.Avium
10	♂,40 yr	neg	–	neg	neg	neg	pos	pos	CTA
11	♀,54 yr	neg	neg	neg	M.Tuber.	neg	neg	pos	M.Tuber.
12	♀,29 yr	neg	neg	neg	M.Tuber.	pos	neg	neg	M.Tuber.

X-ray : chest X-ray
PPD-test : PPD-skin-test
acid-fast : acid-fast-staining of material from the lesion
cultures : cultures of material from the lesion
Ultrasound pos : spread into subcutaneous tissues and/or intranodal calcifications
Cytology pos : granulomatous lesions
Histopathology pos : granulomatous lesions with caseation and necrosis
* type of Mycobacterium not known

Table 2 Results of the diagnostic tests in patients with CTA.

	CORRECT	INCONCLUSIVE	NOT PERFORMED
PPD SKIN-TEST	6	4	2
ACID-FAST STAINING*	3	9	-
CULTURES*	7	5	-
ULTRASOUND	9	3	-
CYTOLOGY	2	4	6
HISTOPATHOLOGY	6	2	4

* Acid-fast staining and cultures were from aspiration biopsy when performed. In the remaining cases these investigations were performed on the surgical specimen.

patients the parotid gland only was affected; in the remaining patients lymph node involvement was established on ultrasound examination: multiple lesions in 7 patients, bilateral lesions in 5, and a single lesion in 2 patients. In patients with multiple lesions, these were generally established at ultrasound only.

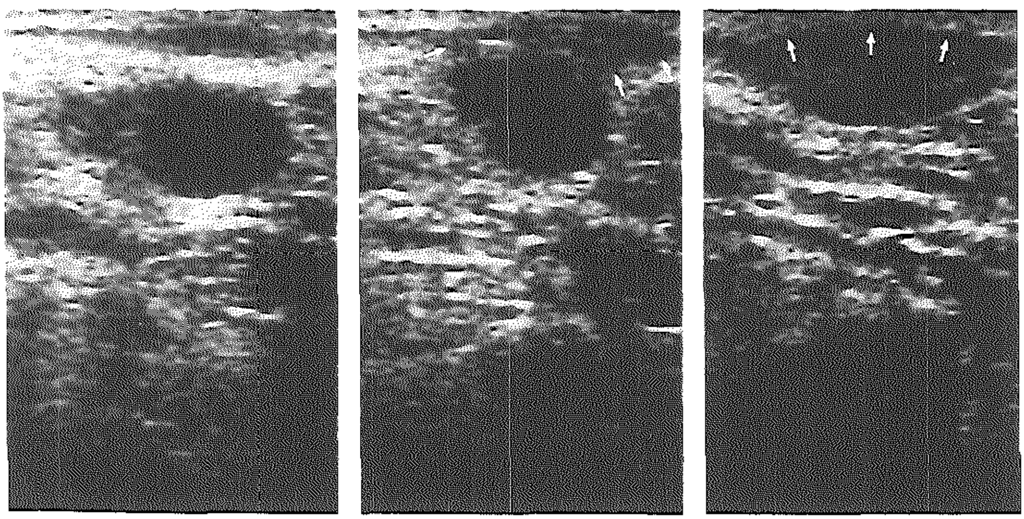

Fig. 1a Slightly enlarged lymph node with non-specific sonographic appearance. The node shows relatively well-defined margins and a low echogenic texture.

Fig. 1b Lymph node with inhomogeneous aspect and irregular borders. Some infiltration of the subcutaneous tissues is present.

Fig. 1c Marked spread into the subcutaneous tissues, seen as a decrease in echogenicity of the subcutaneous tissues.

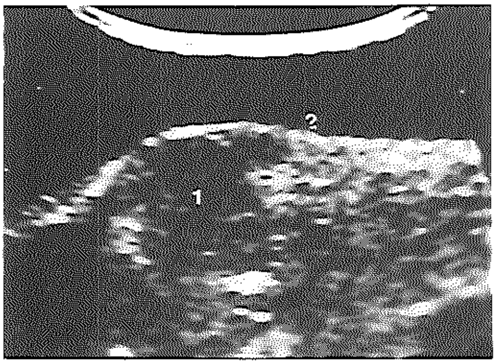

Fig. 2 *Ultrasound appearance of a 'collar stud' abscess in cervical tuberculous adenitis, demonstrating spread into the subcutaeous tissues.*
1 'collar stud' abscess
2 skin

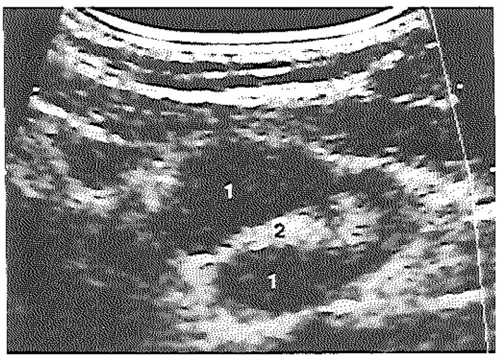

Fig. 3 *Conglomerate nodal tuberculous mass, characterized by low echogenicity with broad, high echogenic, fibrous bands between the nodes.*
1 nodal mass
2 fibrous band

Four different types of lesions were observed on ultrasound examination:

1 enlarged nodes (fig. 1a)
2 nodes with inhomogeneous aspect, irregular borders and posterior acoustic enhancement (fig. 1b and 1c)
3 conglomerate nodal masses with a variable degree of coalescence and spread into subcutaneous tissues (fig. 2 and 3)
4 nodes with calcifications.

All lesions were characterized by low echogenicity.

In accordance with Som[6] and Hamilton Bailey[7], calcifications and spread into the subcutaneous tissues were regarded as positive signs of CTA. When these ultrasound conditions for the diagnosis of CTA are applied, 9 of 12 patients with CTA were correctly diagnosed by ultrasound examination. Three patients had non-specific lymphadenopathy only.
The ultrasound findings in patients with CTA are presented in Table 3.

Table 3 Ultrasound findings in 12 patients with CTA.

	PATIENT	ECHOGENICITY	HOM/INHOM	PAE	REG/IRR	SUBC	CALC	MULT	BIL	CONCLUSION
1	♀, 23 yr	low	inhom	pos	irr	pos	pos	pos	pos	pos
2	♀, 75 yr	low	inhom	pos	irr	pos	neg	neg	neg	pos
3	♀, 50 yr	low	inhom	neg	reg	pos	neg	neg	pos	pos
4	♂, 56 yr	low	inhom	pos	irr	pos	neg	pos	pos	pos
5	♂, 40 yr	low	inhom	pos	irr	neg	neg	pos	pos	neg
6	♀, 7 yr	low	inhom	pos	irr	pos	neg	neg	neg	pos
7	♂, 5 yr	low	inhom	neg	reg	neg	pos	pos	neg	pos
8	♂, 53 yr	low	hom	neg	reg	neg	pos	pos	neg	pos
9	♂, 19 yr	low	inhom	pos	irr	pos	neg	neg	neg	pos
10	♂, 40 yr	low	inhom	pos	reg	neg	neg	pos	pos	neg
11	♀, 54 yr	low	inhom	pos	reg	neg	neg	neg	neg	neg
12	♀, 29 yr	low	inhom	pos	irr	pos	neg	pos	neg	pos

Reg/irr : regular/irregular borders
Subc : spread into subcutaneous tissues
Calc : intranodal calcifications
Mult : multiplicity
Bil : bilateral involvement
PAE : posterior acoustic enhancement

Discussion

CTA has to be differentiated from a variety of exceedingly more frequently occurring other lesions in the neck. Current methods to confirm or exclude CTA are not uniformly reliable[1,2,3,4,5]. Our results demonstrate once more the low level of effectiveness of the diagnostic modalities (Table 1 and 2).

Radiologic features of CTA did not receive much attention in literature and to our knowledge this study is the first to report on the ultrasound manifestations of CTA.

The ultrasound patterns of nodal involvement which were found, may represent different stages of the disease: nodal enlargement is a non-specific effect of inflammatory disease and may represent an early stage. Later on caseation, necrosis and suppuration may occur, which result in an ultrasound appearance of a low echogenic mass with an inhomogeneous aspect, irregular borders and a variable degree of posterior acoustic enhancement. As the disease progresses, conglomerate nodal masses with abscess-formation and spread into adjacent structures may be formed. These ultrasound patterns concur for a great deal with the stages of CTA as described by Hamilton Bailey[7]. There were no fistulas (stage IV according to Bailey) in our patients.

In patients with multiple lesions, different patterns were apparent simultaneously, indicating that cervical lymph nodes may be in different stages of disease in one patient.

Stages of nodal involvement and conglomerate nodal masses in CTA have been described by Reede et al[8]. in their study on CT manifestations of CTA. It is striking that nodal calcifications are not mentioned as a CT manifestation of CTA, since these are reported to be quite characteristic for tuberculosis and other granulomatous disorders[6]. Moreover, the spread into subcutaneous tissues is not mentioned. Presumably, this is because ultrasound examination with small-parts transducers is superior to CT in the assessment of superficial structures in the neck. Figures 3 and 4 illustrate that ultrasound and CT produce similar patterns of conglomerate nodal masses.

Multiplicity and bilateral involvement were often not expected at clinical examination. As may be anticipated from the results in part II, several non-palpable lesions were demonstrated by ultrasound. The establishment of multiplicity and/or bilateral involvement may influence the extent of surgical treatment in these patients.

The sensitivity rate of the ultrasound examination based on the presence of spread into subcutaneous tissues and/or nodal calcifications equalled histopathology, and surpassed the other diagnostic tests. In our 5-year experience with ultrasound examination of the head and neck we encountered spread into subcutaneous tissues only in two patients with cat scratch disease (CSD). Both CTA and CSD are granulomatous disorders which may show a variable degree of necrosis and suppuration of the lymph nodes. This may account for the similarity in ultrasound manifestations.

As most other tests are more time-consuming and the results of ultrasound examination are available without any delay, application of this test to patients with elusive cervical masses

Fig. 4 *Transverse CT view at the level of the mandible. A multichambered, inhomogeneous tuberculous mass is located lateral in the neck. Rims of enhancement are seen within and around the periphery of the mass. The spread into the subcutaneous tissues is indicated by arrows.*
1 tuberculous nodal mass
2 mandible
3 air in the larynx
4 spread into the subcutaneous tissues
5 cervical vertebra
6 neck musculature

may result in earlier recognition of CTA.

Ultrasound examination may be used to follow up patients with CTA: in 3 patients ultrasound examination was used to monitor the effect of chemotherapy. In two of these, ultrasound examination demonstrated response to the administered drugs, and the treatment was continued. In the third patient, ultrasound examination showed no response and the patient was treated surgically.
In case Nr. 6, a parotid tuberculous abscess was demonstrated. Several surgical drainage procedures failed to cure this patient. Excellent results of percutaneous drainage under ultrasound control of para- and retropharyngeal abscesses (part IV), led us to apply this treatment to this patient. Using the Seldinger technique, a pig-tail catheter was inserted into the abscess-cavity. Anti-tuberculous drugs (INH and Kanamycin) were administered through the drain. Repeated ultrasound examination showed gradual improvement and finally complete recovery. This procedure may be an alternative to extensive surgery or systemic chemotherapy.

Conclusions

1 The ultrasound features of CTA are quite distinctive, but may resemble those in CSD.
2 Ultrasound characteristics of CTA are intranodal calcifications and conglomerate nodal masses with a variable degree of coalescence and spread into the subcutaneous tissues.
3 According to the findings at ultrasound, multiplicity and bilateral involvement occur more frequently than expected at palpation.
4 When ultrasound is performed routinely in the evaluation of patients with a cervical mass, ultrasound findings may alert the clinician to the possibility of CTA at an earlier stage.
5 Ultrasound examination may be used to monitor the response to therapy and to follow-up the patient.

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Chapter III.8

Miscellaneous

Introduction

Beside the relatively frequent occurring conditions described in the preceding chapters, there are numerous, mostly rare, disorders which may present to a head and neck surgeon as a head and neck mass. Because of the small number of patients involved, our experience with these disorders is limited. Nevertheless, some of these disorders appeared to produce an interesting ultrasound pattern. These disorders are: dermoid cyst, cystic hygroma, carotid body tumor, carotid aneurysm, ranula, deformity of cervical vertebra, and masseteric hypertrophy. Because recognition of the ultrasound pattern may aid to establish the diagnosis in these conditions, these patterns will be described as follows.
The added information on pathogenesis, epidemiology and clinical pattern is derived from the textbooks of Batsakis[1], Paparella[2] and Thawley[3].

Dermoid cyst

Dermoids are the most common teratoma-like lesions in the neck. They are to be differentiated from simple epidermal inclusion cysts, true teratomas, and thyroglossal duct cysts. Most teratomas are present at birth, whereas dermoids and thyroglossal duct cysts may present later in life. A dermoid cyst may contain a variable number of skin appendages (hair, hair follicles, sebaceous glands, sudoriferous glands) as well as cheesy keratinous material. The dermoid may occur on the forehead, the nose, the brow areas, the occiput, or in the submental area (fig. 1a, 1b). Usually, these cysts are asymptomatic.
Depending on the contents of the cyst, the ultrasound appearance may range from homogeneous to inhomogeneous, and from low to high echogenic. Dermoid cysts may be misinterpreted as solid tumors due to the presence of internal reflections. A cyst with a high echogenic pattern is presented in fig. 1c and fig. 1d. CT (fig. 1e) confirmed the presence of a large cyst in the submental area. The findings at surgery corroborated the relationship to adjacent structures as shown at ultrasound and CT, and explained the high echogenicity of the lesion (fig. 1f).

Cystic hygroma

Cystic hygroma is one of three types of lymphangioma: lymphangioma simplex, cavernous hemangioma and cystic hygroma. The three types of lymphangiomas differ with respect to the size of the vascular spaces and thickness of the adventitia. Cystic hygromas are found predominantly in the neck and are noticed at birth or shortly thereafter. In most cases, the cystic hygroma is located in the posterior triangle of the neck, but larger masses may extend beyond the sternocleidomastoid muscle into the anterior compartment and often cross the midline.
On palpation, a cystic hygroma is usually compressible and may be transilluminated.

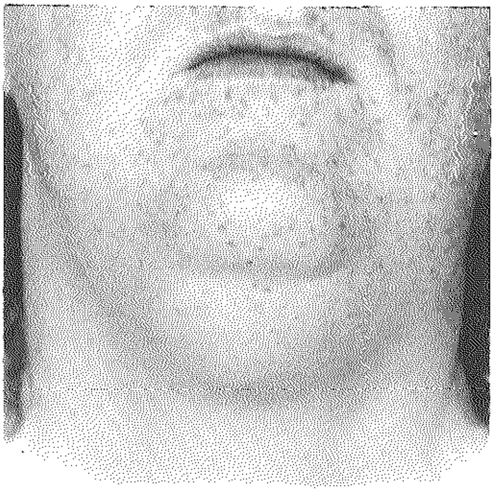

Fig. 1a *Double chin appearance of a large dermoid cyst.*

Fig. 1b *Double chin appearance of a large dermoid cyst.*

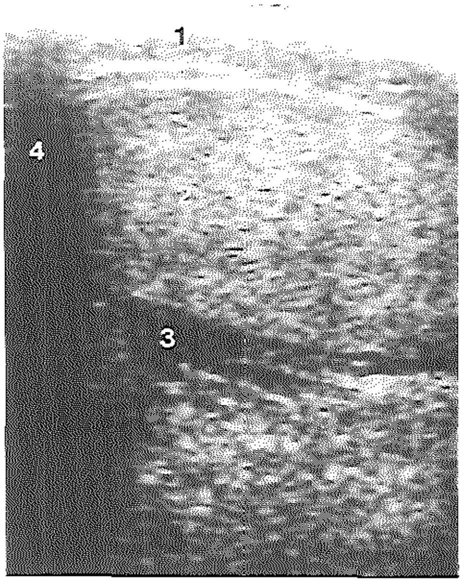

Fig. 1c *Same patient. Longitudinal section of the floor of the mouth, demonstrating a highly echogenic, homogeneous cyst. The subcutaneous fat (1) and the mylohyoid muscle (not shown in this section) are superficial to the mass (2). The genioglossal muscle (3) is displaced, and is located deep to the lesion. The mandible can be recognized by its posterior acoustic shadowing (4).*

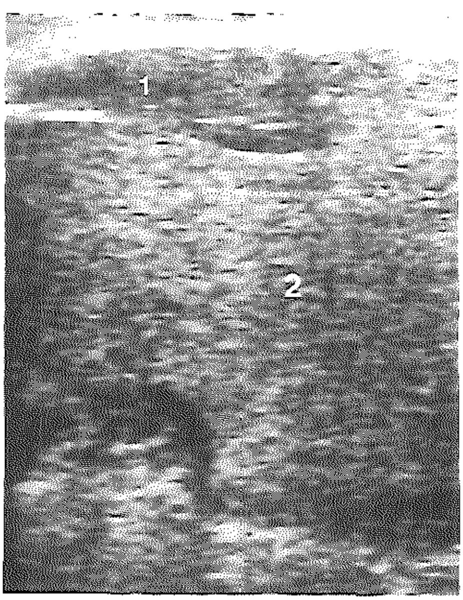

Fig. 1d *Transverse ultrasound section of the floor of the mouth in the same patient. The digastric muscle (1) is demonstrated superficial to the dermoid cyst (2).*

Fig. 1e *CT appearance of the same dermoid cyst. The cyst (1) is well-delineated and characterized by low density. This picture shows the relationship to the digastric muscles (2), the mandible (3), and the base of the tongue (4).*

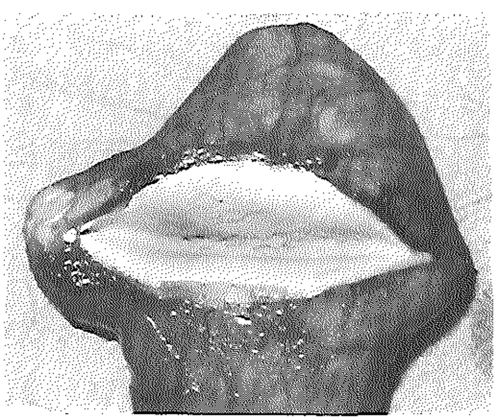

Fig. 1f *Incised dermoid cyst, showing the cheesy contents.*

At ultrasound examination, cystic hygromas are predominantly cystic with septae of variable thickness (fig. 2a, 2b). Our findings concur with the few descriptions of other authors which are available[4,5].

Carotid body tumor

The carotid body is a small, ovoid mass, measuring approximately 5 mm in size and is located at the carotid artery bifurcation. The carotid body responds to arterial changes in pH, temperature, oxygen and carbon dioxide tension and causes reflex changes in respiration and vasomotor activity. The carotid body is usually not depicted by ultrasound.

The carotid body tumor is found predominantly in middle aged patients. The tumor adheres to the carotid bifurcation restricting the mobility in vertical direction at palpation, but the tumor may be moved laterally. A bruit or thrill may be present.

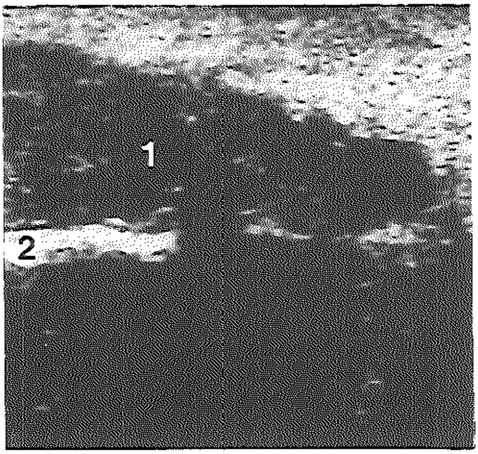

Fig. 2a *Cystic hygroma in the left cheek (transverse view). the mass (1) is superficial to the mandible (2). The lesion shows numerous small cysts separated by high density septae.*

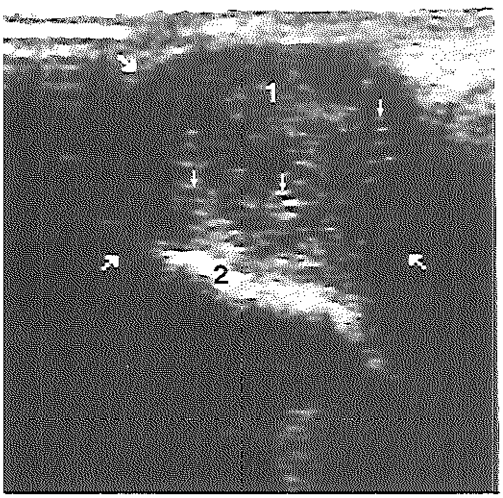

Fig. 2b *Same patient. Oblique view showing tubular structures within the hygroma. Some dilated vessels are indicated by the arrows within the mass (1). Posterior acoustic shadowing of the mandible (2).*

At ultrasound examination, the tumor appeared to be inhomogeneous (fig. 3). The margins may be well- or ill-defined. Characteristically, the tumor is localized between the internal and external branches of the carotid artery. This localization may lead to a displacement of the vessels.

Aneurysms of the carotid artery

A tortuous course or aneurysmal dilatation of the carotid artery may occur in elderly patients and may mimic a solid tumor. The vascular nature of both conditions is clearly demonstrated at ultrasound examination (fig. 4).

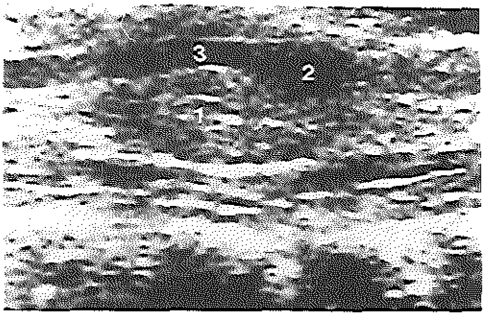

Fig. 3a *Longitudinal view at the level of the carotid bifurcation. A solid mass (1) is situated at the carotid bifurcation (2) displacing the external carotid artery (3).*

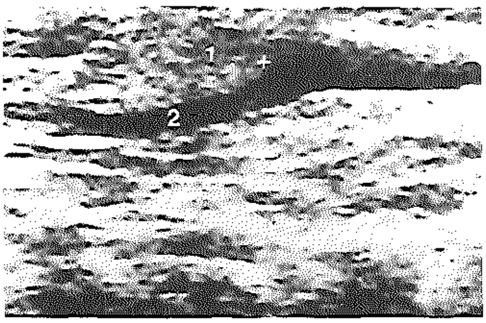

Fig. 3b *Longitudinal view of the carotid body tumor (1) and the internal carotid artery (2).*

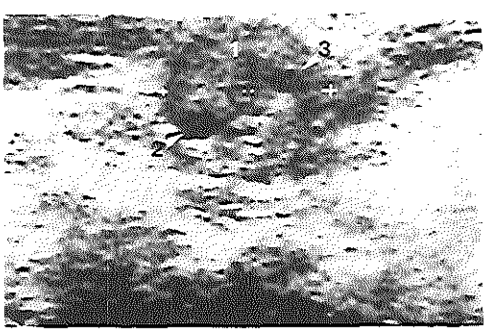

Fig. 3c *Transverse view cranial to the carotid bifurcation. The carotid body tumor (1) is well delineated and is surrounding both the internal (2) and external (3) carotid artery.*

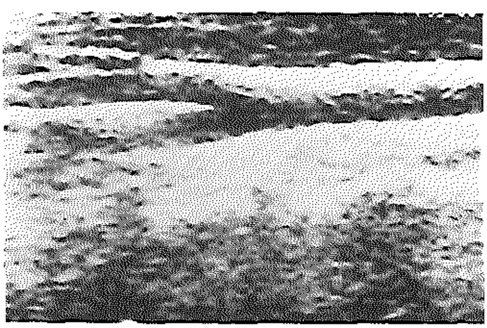

Fig. 3d *Longitudinal view of the normal contralateral carotid artery bifurcation in the same patient.*

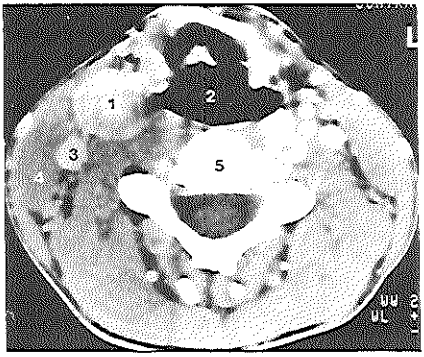

Fig. 3e *Transverse CT section after intravenous contrast medium was injected. The carotid body tumor (1) is recognized as a hyperdense structure. Air in the larynx (2); jugular vein (3); sternocleido-mastoid muscle (4), and cervical vertebra (5).*

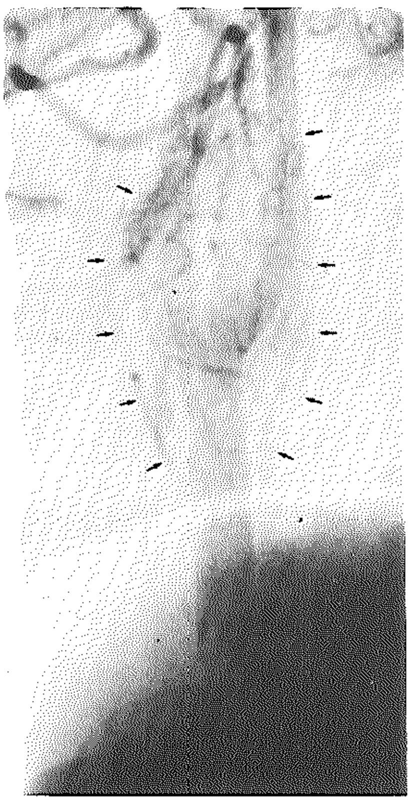

Fig. 3f *The highly vascular nature of the tumor (arrows) as demonstrated by arteriography.*

Ranula

A (simple) ranula is caused by partial obstruction of the distal end of a sublingual gland duct. The dilatation results in an epithelial lined cyst in the floor of the mouth. Disruption of the lining produces a connective tissue lined space. The extravasation pseudocyst can dissect through the mylohyoid muscle to cause a swelling in the neck: plunging ranula.

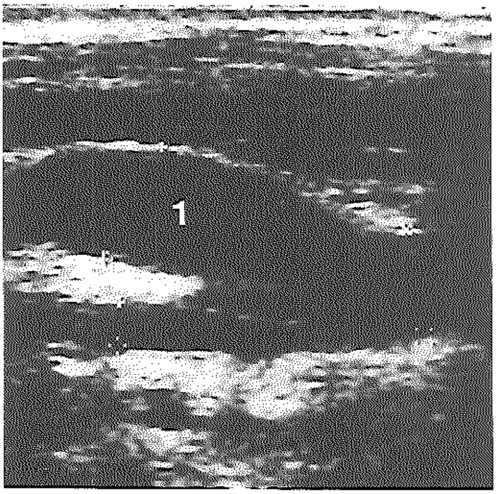

Fig. 4 *Longitudinal ultrasound view of the carotid artery bifurcation. The internal carotid artery shows an aneurysmal dilatation (1).*

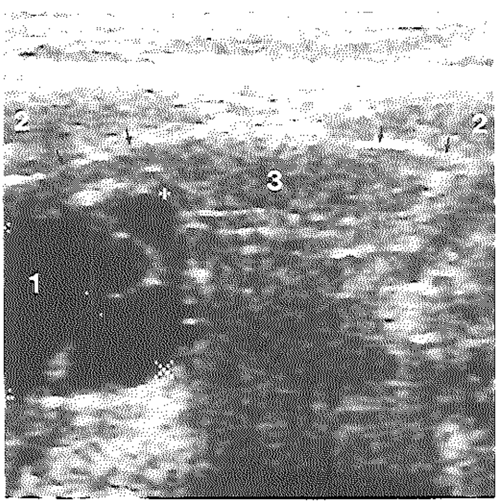

Fig. 5 *Transverse ultrasound view of the floor of the mouth. A simple ranula (1) is located at the oral side of the mylohyoid muscle (arrows). The relationship to the digastric (2) and genioglossal muscles (3) is shown.*

Simple ranulas present as cystic masses in the floor of the mouth, and are usually recognized as such at clinical examination. Ultrasound may confirm the clinical diagnosis by showing a cystic mass, cranial to the mylohyoid muscle (fig. 5).

Plunging ranulas however, are more difficult to establish on clinical grounds. In our limited experience (2 cases), the ultrasound appearance was quite specific: a cystic mass piercing the mylohyoid muscle (fig. 6).

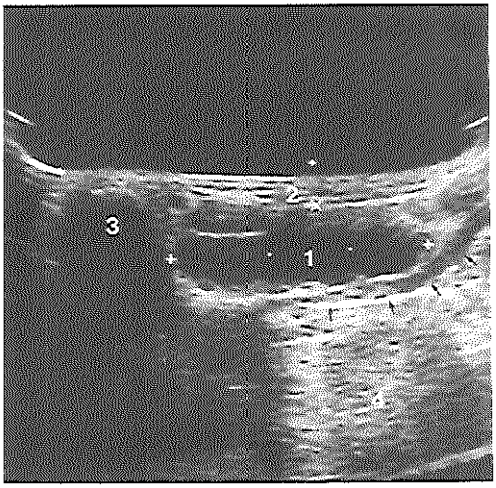

Fig. 6 *Oblique ultrasound view of the floor of the mouth showing a plunging ranula (1). The plunging ranula is located between the subcutaneous fat (2) and the mylohyoid muscle (arrows). The mandible is characterized by posterior acoustic shadowing (3); The base of the tongue is indicated (4).*

Deformity of the cervical vertebra

Ossified ligaments, osteophytes, enlarged transverse processes of the cervical vertebrae, etc., may present as a neck mass. Although ultrasound cannot define osseous pathology, masses can be identified as being bony. An example of a patient presenting with an elusive neck mass, which proved to be osseous in nature, is demonstrated in fig. 7.

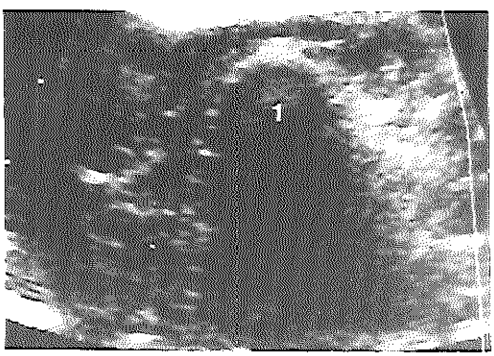

Fig. 7a *A strong reflection (1) with posterior acoustic shadowing at the level of a palpable neck mass in the posterior triangle of the neck, suggestive of osseous pathology.*

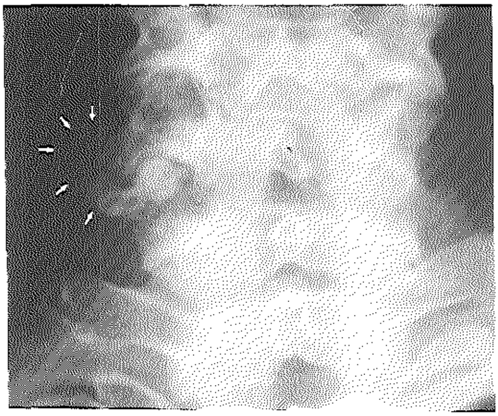

Fig. 7b *Plain radiography confirmed the ultrasound findings, showing a bony deformity of a cervical vertebra (arrows).*

Masseteric hypertrophy

The masseteric muscle is one of the structures in the parotid region which may cause a swelling. Enlargement of the masseter muscle may resemble a parotid mass. Masseteric hypertrophy causes a characteristic ultrasound pattern, which allows differentiation from the specific appearance of parotid gland lesions (chapter III.4-III.6) (fig. 8).

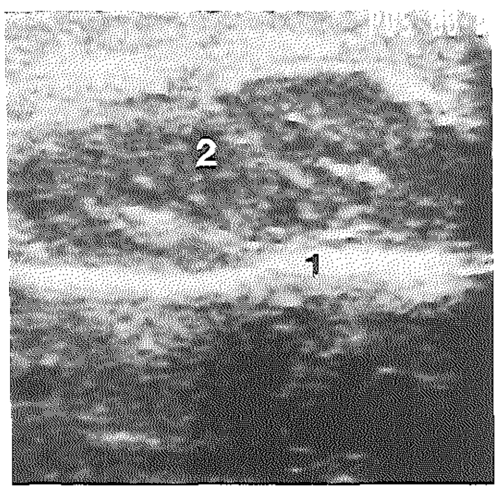

Fig. 8 *Ultrasound view parallel to the mandible (1). The masseteric muscle (2) is enlarged.*

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Chapter III.9

Comment

General aspects

Prior to the start of this study in 1984, only a few reports dealt with ultrasound examination of the soft tissues of the head and neck. At that time the distribution of high frequency transducers, suitable for examination of the superficial structures of the head and neck, was still limited. Moreover, the poor spatial resolution of the then available ultrasound equipment allowed depiction of gross pathology only. Consequently, the value of ultrasound was restricted to the establishment of the cystic or solid nature of a palpable neck mass[1 2 3 4 5 6 7 8].

The diagnostic power of ultrasound in the examination of superficial structures improved greatly after further development of the technical equipment. The increased spatial resolution and the possibility of detailed examination of superficial structures suggested that ultrasound could contribute more substantially to the assessment of head and neck pathology.

While our study was in progress, several reports on the ultrasound pattern of neck masses were published by authors who also used the new generation of ultrasound equipment. Most of these studies dealt with salivary gland disease only[9 10 11 12 13 14 15 16 17 18 19]. Few reports dealt with the application of ultrasound in other pathology of the neck[20 21 22 23 24 25].

A methodical description of the ultrasound images of the normal anatomy and a number of pathologic head and neck conditions was provided by Bruneton in 1987[26] and Czembirek in 1988[27]. In their textbooks the ultrasound pattern of various tumors was considered to be specific. From our observations it was concluded that ultrasound is not suitable for reliable tissue differentiation. This will be discussed in the next section. Nevertheless, we agree with Bruneton and Czembirek that ultrasound may supply substantial information in the work-up of patients with a head and neck mass.

This thesis is based on the first five years (1984 - 1989) of experience with ultrasound examination of the head and neck region in patients referred to the Department of Otorhinolaryngology at the University Hospital Rotterdam. The value of ultrasound in the assessment of cervical metastatic disease was the subject in Part II.

In contrast to most other studies, the sonographer was not acquainted with the results of clinical examination. This was to allow an unbiased judgment of the value of ultrasound in the diagnosis of head and neck pathology.

Ultrasound, which reflects acoustic properties of tissues and organs, produces images of normal and pathological structures in the neck. In our experience, the most important features of ultrasound imaging appeared to be:

1 Although the ultrasound images are two-dimensional, changing the position of the transducer permits a three-dimensional impression of the various structures in the neck (chapter I.3).
2 The ultrasound appearance of these structures is quite characteristic (chapter I.3):
  - muscles are low echogenic, elongated structures, with narrow, high echogenic lines;
  - the thyroid and salivary glands are homogeneous, high echogenic and well-defined structures. These structures, with equal ultrasound pattern, may be differentiated on the basis of their precise localization as depicted by ultrasound;
  - lymph nodes generally are round to ovoid shaped in the jugulo-digastric region, and spindle shaped in the lower regions. They are of varying echogenicity, but mostly low echogenic. Margins are generally well-defined;
  - blood vessels are echo free, tubular, well-defined structures. Pulsatile movements indicate arteries; Valsalva's manoeuvre may be used to identify the jugular vein, and its patency (thrombosis);
  - bony structures and the larynx may be identified by a strong reflection and posterior acoustic shadowing.
3 Lesions as small as 5 mm can be demonstrated (part II and chapter III.5). Lesions may be characterized by shape, the extension, delineation, localization, and topographic relationship to adjacent structures.
4 The size of a lesion can be measured precisely, since the ultrasound equipment is calibrated.
5 Cystic and solid lesions can be differentiated (chapter I.3, chapter III.1, III.2, and III.3).
6 Changes of the parenchymous texture of salivary glands can be shown (chapter III.6).
7 Ultrasound enables controlled aspiration biopsy (chapter I.4).

However, some important limitations of ultrasound emerged:

1 Since sound waves are reflected at interfaces with bone or air, ultrasound does not allow assessment of osseous or air-containing structures. Lesions in the ultrasound shadow of these structures are not visualized (chapter I.3 and III.6).
2 Malignant invasion in adjacent structures is generally not visualized by ultrasound (chapter II.5).
3 Nerves are not demonstrated by ultrasound (chapter I.3 and III.4).
4 Cysts with highly echogenic contents may resemble solid lesions (chapter I.3, III.1, III.8, and III.2).
5 Due to the limited penetration of high frequency transducers, delineation of deep, large lesions is restricted.
6 Ultrasound does not allow tissue diagnosis of pathologic conditions (part II and chapter III.5).

Ultrasound and cytologic examination

Ultrasound

Differentiation between benign and malignant disease in the head and neck region by ultrasound has been a matter of dispute, in particular for salivary gland lesions and cervical lymph nodes.

Delineation and parenchymous pattern have been advocated[13 14 15 16 17 24] and denied[18 19 25] as criteria for such a differentiation in salivary gland disease. It was demonstrated in chapter III.5 that ultrasound examination cannot differentiate between benign and malignant parotid disease. Our series of salivary gland tumors comprised many small lesions (average diameter 2.7 cm for benign, and 1.7 cm for malignant tumors). In most of the small malignant tumors, and benign lesions, a well-defined border was found. Only larger malignant tumors demonstrated ill-defined borders. This suggests that the margins of a malignant tumor become ill-defined with increasing size and increasing infiltration. A larger average diameter of the tumors in the previously mentioned studies could explain the difference with our findings.
An inhomogeneous parenchymal pattern has been suggested to be another feature of malignant salivary gland disease . However, the mixed constitution of benign tumors, e.g. pleomorphic adenoma with small cystic components and a variety of other contents, may account for an inhomogeneous aspect as well.
Thus, delineation and parenchymal pattern are poor predictors of malignancy in parotid gland lesions.

As discussed in chapter II.1, ultrasound cannot discern between benign and malignant cervical lymph nodes either. Bruneton[28] was the only one who claimed a high specificity for cervical metastases. Actually, this high specificity was based on a criterion of size (more than 8 mm in diameter). However, there is evidence from relevant literature that nodes of any size may be metastatically involved (part II). Therefore, we consider the size criterion as a poor predictor of malignancy too.

In conclusion, ultrasound is not suitable for obtaining tissue diagnosis in lymphadenopathy and neoplastic salivary gland disease. It remains to be determined whether the same holds true for tumors of other origin.

Cytologic examination

Many of the lesions demonstrated by ultrasound require cytologic examination for further evaluation. However, the ultrasound pattern of some palpable masses is sufficiently characteristic to make cytologic examination superfluous:

- cystic lesions, which are not recognized as such at clinical examination, are identified at ultrasound with a high degree of reliability. These lesions usually do not require cytologic examination. When cytology is needed, UGFNAB allows selective sampling from solid (wall) and cystic parts;
- diffuse glandular enlargement, which may mimic tumefaction, is readily recognized at ultrasound;
- the carotid bulb may be misinterpreted at palpation, especially in elderly patients. Ultrasound will clearly depict the vascular nature. The same holds true for vascular lesions, such as carotid body tumors and aneurysms, and
- bony structures and muscular masses may resemble pathologic conditions at palpation. Ultrasound examination however, may reveal the true nature.

In the next section the adjunctive value of cytology in the assessment of common head and neck disorders is summarized.

Lymph nodes

In cytologic examination of cervical lymphadenopathy, the main objective is to differentiate between benign and malignant disease. In chapter II.2, the accuracy of cytologic examination in squamous cell carcinoma is outlined. In the head and neck a variety of other malignant tumors may occur. Some of these require further histopathologic examination (lymphoma); others present a cytologically characteristic pattern which allows therapeutic management (adenocarcinoma, undifferentiated carcinoma, melanoma)[29].
In the diagnosis of reactive lymphadenopathy, some pathology may require serologic or bacteriologic confirmation. In other types of inflammation (tuberculosis, aspergillosis), cytologic examination by an experienced cytopathologist may clearly add to the diagnostic process.

Salivary gland lesions

The over-all accuracy-rate of cytologic examination in the differentiation between benign and malignant salivary gland lesions is generally more than 95%, as quoted from the review of the literature on this subject by Layfield et al[30]. Our own results are in accordance (chapter III.5).

Ultrasonically non-encapsulated lesions

This subset of pathology includes, e.g. cysts with highly echogenic contents, neurogenic tumors, mesenchymal tumors. Occasionally, a branchiogenic cyst may present as a non-encapsulated lesion because of its echogenic appearance. The accuracy of cytologic examination in case of branchiogenic cysts is reported to be between 86 and 92%[31 32]. The diagnosis is based on the presence of benign squamous epithelium in the smears. However,

Engzell[3] demonstrated squamous cells without obvious morphologic signs of malignancy in 6% of the smears from carcinoma metastases. Therefore, it is not possible to make a definite differentiation between a congenital cyst of the neck and a squamous cell carcinoma metastasis of the neck from the morphologic appearance of squamous epithelial cells in aspirates. The presence of amorphous debris and cholesterol crystals in the aspirate and history taking and clinical examination may still lead to the correct diagnosis. In case of doubt, histopathologic examination is indispensable.
The cytologic diagnosis of neurogenic tumors is reliable; however, classification and typing of these tumors may be more difficult[33].
Mesenchymal tumors can, in most instances, be separated from neoplasms derived from lymphoid and neural tissue, and melanocytic cells. As most soft tissue tumors derive from and resemble differentiated cells such as fibroblasts, histiocytes, and muscle, fat, or endothelial cells, it is possible to type these tumors[30].

Thyroid disease

Although thyroid disease was excluded from our study, thyroid disorders may present as an elusive head and neck mass. Especially ectopic thyroid tissue may pose a difficult differential diagnostic problem. Cytologic examination will usually reveal normal thyroid contents. Cysts and neoplasms may be identified by cytologic examination with a high degree of reliability[34 35 36 37 38 39].

The aforementioned studies dealt with cytologic examination of material obtained by FNAB. The results discussed in chapter II.2, indicate that UGFNAB may be more efficacious than FNAB. This is probably due to the constant visualization of the tip of the needle and the lesion during aspiration, and to the controlled sampling of different areas with this technique. It can be speculated that the efficacy of UGFNAB in other lesions may compare favourably with FNAB too.

Validity

To judge the validity of ultrasound as a diagnostic method, the bias which may have occurred during our study, has to be considered. Several types of bias may apply to this study.

Spectrum bias may occur when the patient sample does not include an appropriate spectrum of mild and severe, treated and untreated disease, as well as individuals with commonly confused disorders. The patient populations visiting a University Hospital or a General Hospital are certainly different. In a University Hospital more unusual and probably more severe pathology may be encountered. In populations in which the pathology is less severe, the ultrasound pattern may be less clear-cut, and ultrasound may appear less sensitive.

The proportion of patients with reactive lymphadenopathy in our study, is probably lower than in a General Hospital. An increase in the number of reactive lymph nodes may increase false positive rates for certain pathologic conditions.
Lesions with an obvious clinical diagnosis as sebaceous cysts and lipomas, were not referred for ultrasound examination, and did not enter the study. These lesions might have caused interpretive confusion as well.
On these grounds, it might be anticipated that in populations with a lower incidence of the conditions which were studied, the sensitivity and specificity rates are lower.

Verification bias occurs when not all test results are verified. Patients with a negative result of ultrasound for the condition for which they were tested, were less likely to be referred for verification. Since only verified cases were included in our study, our series comprises a comparatively low number of true negative and false negative results.

Test-review bias does not apply to ultrasound examination in this study: ultrasound examination was performed without clinical information or the results of other diagnostic tests. However, the information achieved by history taking may have influenced the interpretation of palpation. Therefore, the results of palpation in our study may have been biased.

Observer variation is an important determinant of validity too. Since ultrasound examination of the head and neck requires considerable experience, we have the impression that the results are dependent on the competence of the sonographer. A thorough training and a close cooperation with the surgeon and the cytopathologists may reduce interobserver variability.

Ultrasound examination in the work-up of an elusive neck mass

Careful history taking and physical examination may supply a diagnosis in patients presenting with a mass in the head and neck region. As the interpretation of palpatory findings is quite difficult (e.g. branchiogenic cysts (chapter III.2), laryngoceles (chapter III.3)), the clinical diagnosis will be associated with uncertainty. Usually, this uncertainty is determined by the obscure characteristics of the lesion (cystic, solid, bony), or lack of clarity regarding the exact topographic relationship of the lesion.
Currently, various diagnostic tests may contribute to the diagnosis. Plain radiography may be employed in sialo-lithiasis, dental and osseous disease, and can be used to demonstrate the width of the pre-vertebral space in retropharyngeal abscesses. Sialography may be applied in the work-up of non-neoplastic salivary gland disease. However, sialography is contra-indicated in acute sialo-adenitis. Sometimes it is impossible to cannulate the duct.

Conventional tomography can be used for evaluation of intralaryngeal masses. Angiography is necessary to evaluate the arterial system of the neck when vascular lesions are suspected. However, angiography is associated with some morbidity, and even mortality.
The above mentioned imaging techniques share the drawback of a limited field of application. As it is not always clear at presentation which tests should be used, the diagnostic work-up may be inefficient and thus too extensive, or too time-consuming. CT, MRI, and ultrasound are uniformly applicable in the assessment of head and neck masses. Unlike ultrasound, CT and MRI permit evaluation of most primary tumors of the upper-aerodigestive tract, and deep lesions. Osseous pathology is assessed by CT only.
As was demonstrated in this study, ultrasound (with UGFNAB) may provide the correct diagnosis in many head and neck masses. Consequently, the need for other (more expensive) imaging techniques is reduced when ultrasound is used as the initial diagnostic procedure. The use of CT, sialography, etc., may be limited to those cases where ultrasound falls short: e.g., deep neck lesions, large tumors which cannot be delineated in all three dimensions, suspicion of invasion into adjacent structures, salivary gland pathology without abnormalities at ultrasound. In this way a cost effective diagnostic work-up may be accomplished.

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Addendum part III

Guidelines for the use of ultrasound in the head and neck

Submental region

Differential diagnosis

* lymphadenopathy
* dermoid cyst
* thyroglossal duct anomaly
* plunging ranula
* soft tissue tumors

Masses in the submental region are rare, and the differential diagnosis is limited. In general, palpation cannot differentiate reliably between a lymph node, a dermoid cyst, a thyroglossal duct anomaly, and a plunging ranula. Fluctuation may be of help, but is a rare phenomenon. It may indicate a cyst or an abscess.

The property of ultrasound to reveal the solid or cystic nature of a structure will help to differentiate masses. Solid lesions in the submental regions will generally be lymph nodes. Ectopic thyroid tissue is rare in the submental region, and is characterized by a high echogenic appearance rather than low echogenicity, as in lymph nodes. Lymphadenopathy may require (UG-)FNAB.

In cystic lesions the demonstration of a relationship to the hyoid bone, and/or an associated tract, may indicate a thyroglossal duct cyst (chapter III.1). In case of a suprahyoid cystic structure, a thyroglossal duct cyst will be mostly localized superficial to the mylohyoid muscle (which is generally well visualized at ultrasound examination), whereas a dermoid cyst is more often situated at the oral side of the mylohyoid muscle[1,2]. Exceptions to this general rule may occur according to Batsakis[3], and occasionally a dermoid cyst may be located between the platysma and the mylohyoid muscle. Echogenicity may give a clue in these latter cases: dermoid cysts have more or less solid contents[2], whereas thyroglossal duct cysts more often have liquid contents.

A plunging ranula has a cystic appearance too, and is characteristically located superficial and deep to the mylohyoid muscle, piercing this mylohyoid muscle (chapter III.8). In these lesions there is no relationship with the hyoid bone.

Finally, some patients may present with a submental mass, which is considered to be of neoplastic origin clinically. In some of these patients, ultrasound may demonstrate a large volume of subcutaneous fat only, as occurred in some of our patients. Tumefaction was excluded on the basis of these findings.

Anterior neck region

Differential diagnosis

* thyroglossal duct anomaly
* external laryngocele
* branchiogenic cyst or fistula
* dermoid cyst
* lymphadenopathy
* thyroid gland pathology
* soft tissue tumors

Palpation is often indistinct in this area:
Small cystic masses, such as a thyroglossal duct cyst, a fluid-filled laryngocele, a branchiogenic cyst, or a dermoid cyst may be firm on palpation on account of the capsule. The localization of the lesion may sometimes allow differentiation, but a precise estimation of the relationship to adjacent structures, often proves impossible.
By the direct visualization of the lesion and surrounding structures, ultrasound can differentiate between a thyroglossal duct cyst, a fluid-filled laryngocele and a branchiogenic cyst, by determining the localization of the mass near the hyoid, the thyrohyoid membrane and the anterior border of the sternocleidomastoid muscle, respectively.
Additional information may be obtained by asking the patient to swallow while the ultrasound examination is in progress.
The thyroid gland is a well-defined structure at ultrasound examination, with a homogeneous, high echogenic parenchymal pattern. Focal lesions (solid or cystic) or a diffuse enlargement of the gland can be depicted with ultrasound examination.
The indication for (UG-)FNAB in the anterior neck region is limited to some cases of lymphadenopathy, focal lesions of the thyroid, and indistinct cases.
Identification of an external laryngocele at ultrasound, reduces the small risk on a laryngopyocele when a laryngocele is accidentally aspirated following an inconclusive clinical examination.

Submandibular region

Differential diagnosis

* salivary gland disease
* lymphadenopathy
* soft tissue tumors

In this region difficulties in palpation arise as a result of the proximity of the mandible. A differentiation between the submandibular gland and lymph nodes may not be possible.

At ultrasound however, the submandibular gland is well delineated, allowing differentiation between intra- and extraglandular disease. In case of salivary pathology, the etiology may be established at ultrasound examination (e.g. mass lesions, suppurative sialo-adenitis, sialolithiasis, enlargement of the gland due to obstruction of the main duct by carcinoma in the floor of the mouth (chapter III.6)).
Chronic sialo-adenitis may require sialography.

Jugulo-digastric region

Differential diagnosis

* lymphadenopathy
* salivary gland disease
* vascular anomalies
* branchiogenic cysts and fistulas
* soft tissue tumors

The jugulo-digastric region is probably the most confusing region in the neck. The multitude of structures and pathology, and the limited accessibility make this region difficult to evaluate by palpation.
Firstly, the structures which are present in a normal neck are often difficult to distinguish, and may mimic pathologic conditions: the parotid gland, reactive lymph nodes, muscles, blood vessels, or a transversal process of the first cervical vertebra. As discussed previously, ultrasound permits a direct visualization and identification of these structures.
Focal, solid lesions may be attributed to the parotid gland, lymph nodes, or to other structures of the neck at ultrasound examination. As discussed in previous sections, ultrasound can show a characteristic pattern in these cases. Ultrasound findings may be supplemented with cytologic examination when desired.
In general, cystic lesions may be lymphangiomas (e.g. cystic hygroma), cysts in the parotid gland, or branchiogenic cysts. Intra-parotid cystic lesions generally are Whartin's tumors. (UG-)FNAB may confirm this diagnosis. The characteristic pattern of branchiogenic cysts was described in chapter III.2; the appearance of cystic hygroma was outlined in chapter III.8.

Like palpation the ultrasound examination may be hampered by the mandible, especially in respect to masses which extend medially. Furthermore, the limited penetration of the high frequency ultrasound transducers hinder the examination of the medial extension of large tumors. Factors which influence the quality of palpation, such as abundant adipose or muscular tissue may interfere (to a lesser degree) with ultrasound examination also. CT is not interfered by these factors and is indicated when the diagnosis still remains uncertain, or when ultrasound cannot delineate a mass in all three dimensions.

Jugular region

Differential diagnosis

* lymphadenopathy
* vascular anomalies
* branchiogenic cysts
* laryngoceles
* soft tissue tumors

Masses near the carotid bulb may cause specific problems in clinical evaluation. A pulsating mass may be due to an aneurysm, but a lymph node too may be interpreted as such on account of transmitted pulsations. Branchiogenic cysts, external laryngoceles, and lymph nodes may be confused at palpation too.
Vascular lesions on one hand, and nodal disease on the other, can be easily distinguished at ultrasound examination. Because of their cystic nature, branchiogenic cysts, cystic hygroma, and laryngoceles may be identified at ultrasound.

Masses may arise in the posterior triangle of the neck, but these are quite rare. In general, these are soft tissue tumors. The patients with palpable pathology in the supraclavicular region, are generally referred to the general surgeon, or to the department of Internal Medicine, and were therefore not included in our study.
A variety of soft tissue tumors may arise in any region of the head and neck. These tumors include dermoid cysts, lymphangiomas, neurogenic tumors, sarcomas, lipomas, etc. Their localization in or near the structure they originate from (as demonstrated at ultrasound) may help to reduce the differential diagnosis. Ultrasound may also produce measurement of size and delineation of these lesions. When tissue diagnosis is necessary for further management, cytological examination is mandatory.

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PART IV

Ultrasound guided percutaneous drainage of deep neck abscesses

Abstract

Deep neck abscesses may still result in significant morbidity and mortality. Surgical therapy carries the risk of damage to cranial nerves and arteries. Excellent results of ultrasound guided percutaneous catheter drainage of abdominal abscesses led us to apply this technique to the management of deep neck abscesses. Five patients were treated with ultrasound guided catheter drainage and antibiotics. All patients were cured without complications or recurrences. We consider this highly effective treatment as a valuable alternative to conventional therapy.

Introduction

Deep neck space infections affect fascial compartments of the neck and their contents. These infections originate from odontogenic or upper respiratory foci. Antibiotic therapy is often adequate in dealing with uncomplicated upper airway infection as well as deep neck infection[1]. Surgical intervention is indicated only when an abscess is established, but abscesses in the neck are often very difficult to distinguish from other types of inflammation. Ultrasound can be helpful in this respect[2].

Surgical drainage of an abscess in the neck is hazardous with a risk of damage to blood vessels and nerves. This, and the good results of ultrasound guided percutaneous catheter abscess drainage in other areas such as the abdomen[3] led us to apply this technique to the head and neck region.

In this communication we report the results of percutaneous catheter drainage in five patients with an abscess in the neck.

Methods

Clinical examination, laboratory studies, plain radiography, CT and ultrasound examination demonstrated a deep neck abscess in five patients. Each patient was examined by ultrasound on admission and an ultrasound guided puncture was performed for cultures and Gram-stain.

Abscess-formation was established either on admission or after several days of treatment with antibiotics alone. Once an abscess had been demonstrated, it was percutaneously drained under ultrasound guidance by a double-lumen-drain (JSL).

The Seldinger technique (fig. 1) was used to introduce the drain. In three patients the initial puncture was performed with a 22 Gauge needle, in two others with a 18 Gauge needle. The abscesses were drained by 12 French double lumen catheters in all patients.

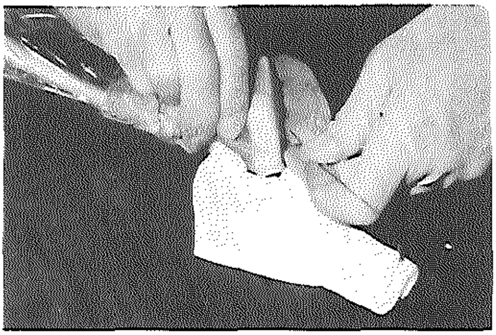

Fig. 1a Ultrasound guided drainage of a neck abscess using the Seldinger technique. A 22 G Chiba needle, packed in a sterile bag, is used.

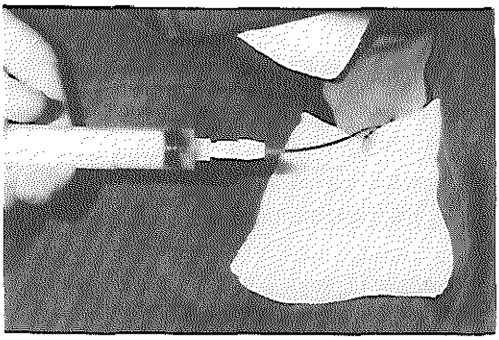

Fig. 1b After inserting a .018 inch guide wire into the needle a 6.3 French catheter is placed in the abscess cavity. Pus is aspirated through the drain.

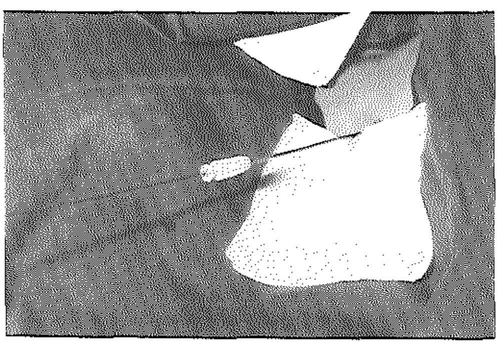

Fig. 1c The catheter permits the introduction of a stiff .035 inch guide wire, which is needed for inserting the thick (12 French) double lumen drainage catheter.

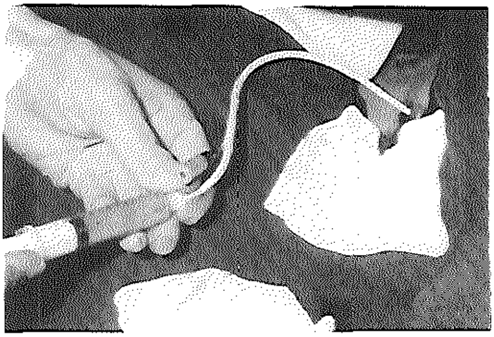

Fig. 1d After dilatation of the canal the double lumen catheter is inserted over the guide wire. Pus is aspirated through the drain.

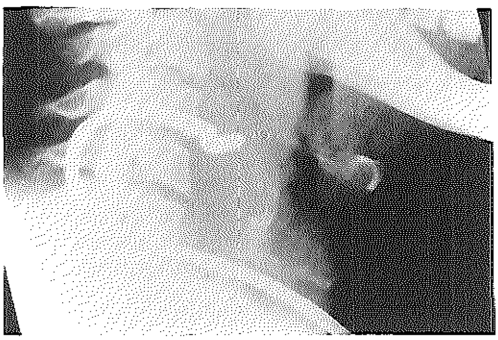

Fig. 1e Lateral X-ray view of the neck. The tip of the catheter is in the prevertebral abscess.

Following drainage, the abscess-cavity was irrigated once a day with a saline solution until the wash-out was clear. In addition, all patients were treated with antibiotics.

Patients

Between July 1986 and April 1987 five patients with a para- and/or retropharyngeal abscess were treated with percutaneous drainage and antibiotics.

Two of the patients had developed complaints after ingestion of a piece of bone. One patient sustained neck trauma the week before. In another case abscess-formation was caused by an infected laryngocele and in the last case (a patient with diabetis mellitus) a specific cause could not be established.

Except for a young boy in whom strangulation had been attempted the week before, all patients were middle-aged or elderly. These patients suffered from one or more of the following diseases: diabetes, chronic heart disease, hypertension or chronic bronchitis.

Case histories

Case 1

A 54-year-old woman with a long history of hoarseness developed a sore throat and progressive dysphagia.
Physical examination showed a very sick woman with a non-fluctuant neck mass on the left, diffuse laryngeal edema and a protrusion of the laryngeal wall.
Plain radiography showed an enlarged prevertebral space. An accumulation of fluid behind and lateral to the pharynx was shown by ultrasound (fig. 2). The abscess was drained under ultrasound guidance. There was discharge of pus for 12 days.
During recovery, both ultrasound and CT showed an internal laryngocele. The course of the disease was uncomplicated and the laryngocele disappeared during follow-up.

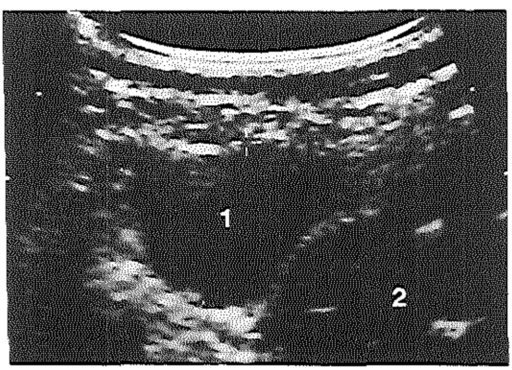

Fig. 2 Fluid filled area based on an abscess-cavity adjacent to the pharynx shown by ultrasound (longitudinal view; case 1).
1 abscess
2 pharynx

Case 2

An 80-year-old female diabetic was admitted to our hospital with a parapharyngeal abscess. Antibiotic therapy for 14 days had failed to cure the patient.
This very sick woman had a swelling of the lateral pharyngeal wall, pus coming from the right parotid duct and right external auditory canal, vocal cord paralysis and paresis of the hypoglossal and accessory nerves.

Both CT (fig. 3) and ultrasound examination demonstrated a large parapharyngeal abscess. Percutaneous drainage resulted in purulent discharge for 12 days and recovery. After 2 months neurologic deficits had disappeared.

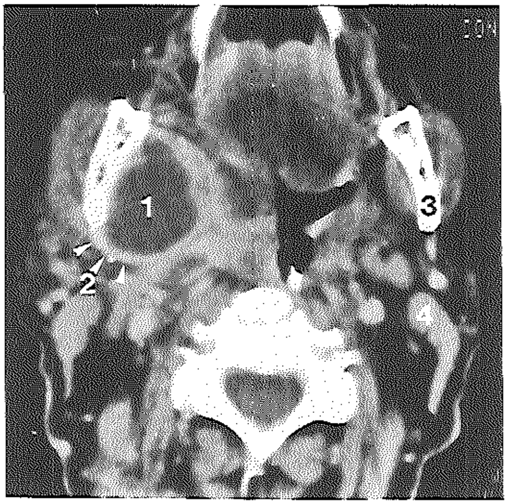

Fig. 3a Transverse CT section of a parapharyngeal abscess before ultrasound guided catheter drainage. An encapsulated area with low density, on the basis of fluid, adjacent to the ramus of the mandible.
1 abcess cavity
2 capsule
3 mandible
4 sternocleidomastoid muscle

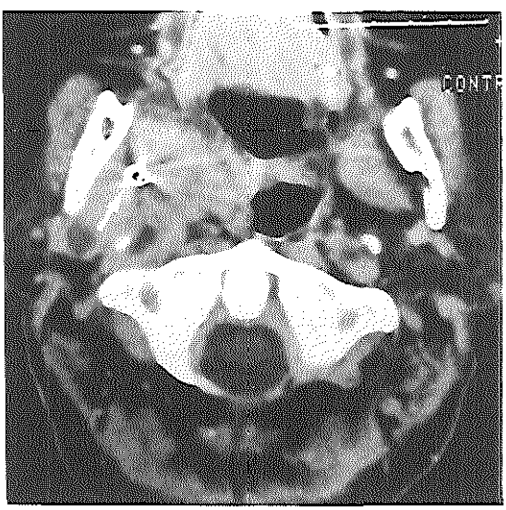

Fig. 3b Same patient; parapharyngeal abscess with double lumen drain in situ (arrow). In comparison to the predrainage view a different scanning direction is used, leading to a different image of the soft and bony tissues in this patient.

Case 3

One week after attempted strangulation, a 15-year-old boy developed dysphagia and pain in the neck.
The boy had high fever, hoarseness, swelling of the posterior pharyngeal wall, and torticollis. The prevertebral space was enlarged on plain radiography. On ultrasound examination there was a fluid collection medial and posterior to the carotid artery (fig. 4). The abscess was

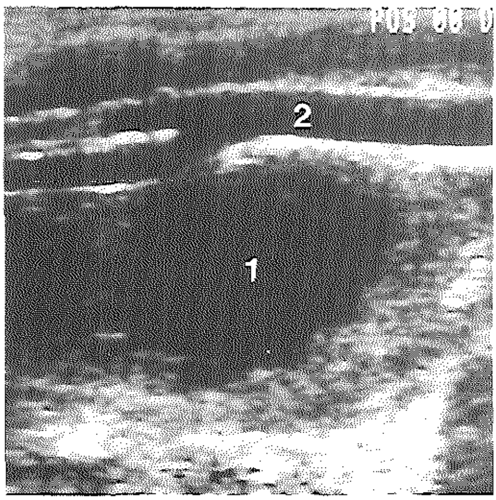

Fig. 4a Longitudinal ultrasound view at the level of the carotid artery. A parapharyngeal abscess is shown as an ill-defined, fluid filled structure medial and dorsal to the carotid artery.
1 abscess
2 carotid artery

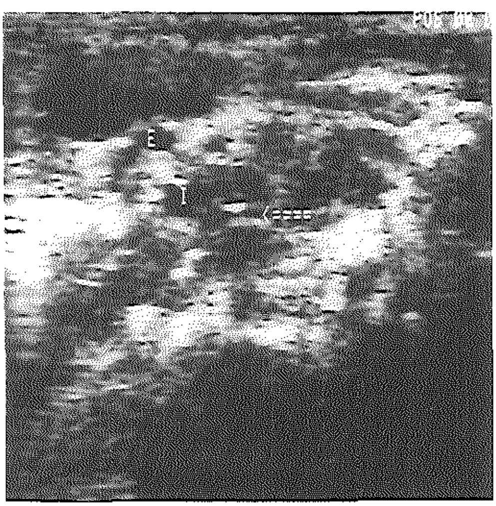

Fig 4b Parapharyngeal abscess with double lumen drain in situ (transverse view). The drain is indicated by an arrow.
I = internal carotid artery
E = external carotid artery

drained. Ultrasound was repeated after one week and showed no signs of pus collection. The drain was removed and recovery was uncomplicated.

Case 4

A 67-year-old man was treated in a neighbouring hospital for a parapharyngeal abscess which developed after ingestion of a fish bone. Despite antibiotics and repeated incision of the pharyngeal wall, this patient did not recover and was admitted to our hospital.
Physical examination revealed a sick man with a non-fluctuant neck mass on the left. Incised pharyngeal mucosa and a displaced pharyngeal wall were seen at laryngoscopy.
Ultrasound examination showed a parapharyngeal abscess while CT showed a cervical mass containing air-bubbles.
After insertion of a drain, pus drained for a week. The patient was discharged in good health after 3 weeks.

Case 5

Following ingestion of a piece of bone, a 54-year-old female diabetic developed dysphagia and dyspnoea.
On intra-oral inspection bulging of the posterior pharyngeal wall was seen.
CT showed a retropharyngeal abscess, which could be confirmed neither by ultrasound examination nor endoscopic investigation with puncture under general anaesthesia. The patient was treated with antibiotics only, but showed no improvement. Repeated ultrasound examination and an ultrasound guided puncture after one week of treatment gave evidence of abscess formation.
Subsequent drainage resulted in discharge for 3 weeks and an uncomplicated recovery.

Results

In all patients the diagnosis was confirmed by a positive puncture under ultrasound guidance. The purulent discharge varied from 7 to 21 days. Despite advanced age and the poor general health of four of our patients, recovery was uncomplicated. No recurrences were encountered during follow-up (18 to 27 months).

Discussion

Deep neck space infections, and especially abscesses in the neck, may still result in significant morbidity and mortality despite the use of antibiotics. Sepsis, dysphagia, dyspnoea, pulmonary complications, mediastinitis etc. may occur.
The evaluation of inflammatory neck masses has proved to be very difficult. The important decision whether to manage these lesions surgically or with antibiotics often rests on physical examination alone, which is not sensitive and nonspecific. This statement is confirmed by our

own findings: no patient had clinical signs of abscess formation. Although CT is quite sensitive as far as the detection and assessment of neck masses is concerned, this technique often fails to detect initial stages of abscess formation.

Ultrasound examination of the neck was improved after the introduction of small parts transducers. This equipment offers high resolution for superficial structures[4,5] and improved differentiation between solid and cystic structures. In our patients ultrasound examination proved to be very helpful in this respect.

Ultrasound guided percutaneous catheter drainage for abscesses is a new technique. The largest experience with this technique has been achieved in the treatment of abdominal abscesses. Overall cure rates of 75% are reported[3]. The results are better for simple, unilocular abscesses and are worse in the presence of multiple abscesses or fistulas. Complications can be avoided by choosing a safe puncture route using CT and ultrasound guidance. The high cure rate, low morbidity and low mortality compared to surgical drainage of abdominal abscesses have resulted in broad acceptance of this technique by general surgeons.

We introduced percutaneous drainage of deep neck abscesses because surgery of an inflammatory neck mass is difficult and carries the risk of damage to the carotid arteries and its branches, the jugular vein, and the cranial nerves. Puncture of the abscess is performed under ultrasound vision. Vascular structures are easily avoided. With the small needles we used, damage to cranial nerves is not very likely and did not occur in our series. Once the correct position of the needle is confirmed by aspiration of pus the introduction of the catheter over a guide wire will cause no additional damage to neighbouring structures.

In our small series of patients we had no complications. Three patients were cured within two weeks and two in three weeks. This somewhat prolonged course might be due to the old age and poor general health of four of our patients. Because of limited experience with this new procedure the drains were left in situ several days after discharge had ceased. This might be another reason for prolonged hospitalisation, and will be changed in future.

Treatment of deep neck abscesses with drainage under ultrasound guidance proved to be safe, quick, and reliable. During the follow-up no recurrences or complications were encountered. Because of these advantages and the favourable results of this treatment, we consider it a valuable alternative to conventional therapy.

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PART V

Final remarks

Unlike the images of CT and MRI, which are made in a standardized way, ultrasonograms are a reflection of a single moment in a dynamic study. The diagnosis is made during the examination and only the most interesting findings will be captured on hard copy. Together with the fact that the position of the transducer is not always obvious on sonograms, the interpretation of the images is difficult for persons other than the sonographer.
Diagnostic ultrasound is not a standard procedure but an interactive process: the images which are obtained during the procedure influence the interpretation of the next images. Each step in the diagnostic process is influenced by the preceeding observations. Therefore, sonography is highly subjective: the quality of the examination is entirely dependent on the skills of the sonographer.

For optimal results of the ultrasound examination the communication between the sonographer and the clinician should be as extensive as possible:
- adequate clinical information;
- explicit presentation of the question;
- standardized reports by the sonographer, including the findings in all neck regions on both sides of the neck, and, very important, also including negative findings;
- size and nature of the lesion, and relationship to adjacent structures should be mentioned.

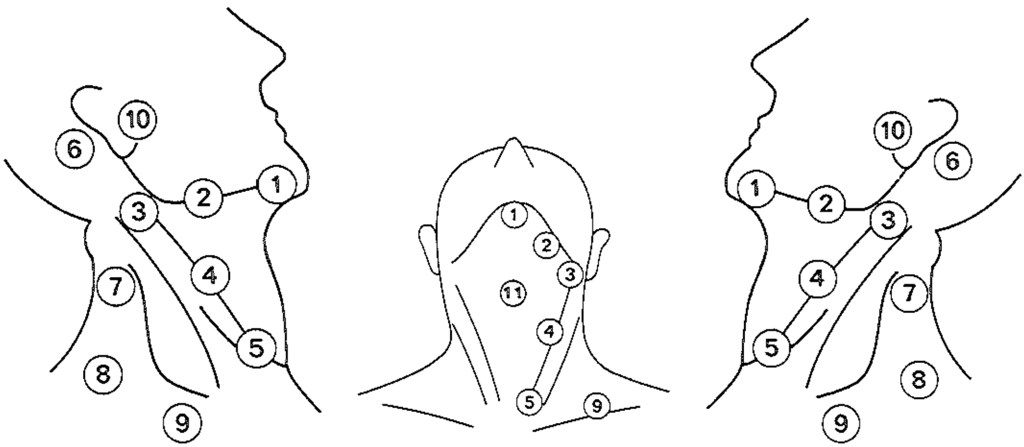
Several conditions may influence the quality of image and examination, e.g. scar formation, irregularities of the skin and an unshaved skin. The presence of a beard hampers the investigation.

A routine ultrasound examination of the head and neck takes about 10 minutes. The procedure, with or without UGFNAB, is much better tolerated than CT and MRI: latter imaging modalities require a certain degree of immobility, including the holding of the breath and refraining from swallowing, during the procedure. These conditions may be very stressful for elderly patients and patients with upper aero-digestive tract cancer. Furthermore, unlike CT and MRI, there is no need for the administration of (intravenous) contrast medium.
Ultrasound may be employed as a bed-side procedure which allows examination on wards or intensive-care units. The conditions during ultrasound examination, e.g. allowing conversation during the investigation, are causing less stress to the patient compared to CT and MRI.
UGFNAB is tolerated very well and more or less as painful as a venous puncture.

Finally, ultrasound examination is not associated with radiation exposure and no side-effects are known. As far as UGFNAB is concerned, there are no (major) complications attributable to the aspiration (chapters I.2 and I.4).

Appendix A

Regions of the neck



1 **Regio submentalis**

Submental nodes are located in the triangle bordered by the anterior bellies of the digastric muscles and the hyoid bone.

2 **Regio submandibularis**

Submandibular triangle nodes lie along the lower border of the mandible. In this study buccal nodes are included in this region.

3 **Jugulo-digastric/subdigastric region**

Subdigastric nodes are located below the posterior belly of the digastric muscle to the level of the greater cornu of the hyoid bone and include the jugular as well as the tonsillar nodes. Retromandibular and parapharyngeal nodes are included in this study.

4 **Mid jugular region**

The mid jugular nodes are along the the jugular vein at the level of the bifurcation of the common carotid, just below the hyoid bone. Parapharyngeal nodes at this level are included in the present study.

5 **Low jugular region**

Low jugular nodes are located along the internal jugular vein just above the anterior belly of the omohyoid muscle.

6 **Upper posterior cervical region**

Upper posterior cervical nodes lie at the upper end of the spinal accessory nerve. The uppermost node is beneath the sternocleidomastoid muscle at the tip of the mastoid process.

7 **Mid posterior cervical region**

Mid posterior cervical nodes include those of the spinal accessory chain at the same level as the mid jugular nodes.

8 **Low posterior cervical region**

Low posterior cervical nodes are located at the lower end of the spinal accessory nerve.

9 **Regio supraclavicularis**

Supraclavicular nodes are located just above the clavicle. This transverse chain connects the jugular and spinal accessory chains.

10 **Regio pre-auricularis**

Pre-auricular nodes are in and around the parotid gland.

11 **Regio anterior**

Prelaryngeal and paratracheal nodes.

Appendix B

Glossary of ultrasound terminology

Absorption	The loss of energy of an ultrasonic wave by its conversion in another form of energy, usually heat. This leads to a display with less intensity of deeper located structures.
Attenuation	The process of decreasing the intensity of an ultrasonic pulse by absorption and scattering.
Axial resolution	The capability of resolving 2 points situated in the axis of the ultrasonic beam.
Echogenic	The extent of reflections caused by the amount and character of the interfaces of structures with a different acoustic impedance.
Echo free	The ultrasound beam is easily transmitted through a structure, the received echoes are below the threshold of the display, so that a black structure is seen on the display.
Frequency	The number of cycles.
Gain	The degree of amplification of the input signal of a device.
Gray scale	Echo reflections will be displayed on a monochrome monitor in different gray shades dependent on the intensity of the reflection.
Impedance	Determined by the product of the density of a tissue and the speed of sound in that tissue.
Lateral resolution	The capability of resolving 2 points in a plane directly perpendicular to the ultra-sonic beam.
Piezo-electricity	The property of material used in ultra sound transducers whereby an electric field is converted to an ultrasound beam and v.v.
Posterior acoustic enhancement	The bright-up zone distal to a zone which enhancement transmits the ultrasonic beam easily, as in echo free zones.

Real-time	A sequence of ultrasound images which gives the impression of a moving picture.
Resolution	See axial and lateral resolution.
Scattering	The redistribution of energy in an ultrasonic wave in all directions by small particles.
Shadowing	The black shadow which is seen behind a strongly reflecting (or attenuating) structure.
Transducer	A device which converts one form of energy into another. See also piezo-electricity.

Appendix C

Glossary of statistical terminology

TEST	GOLD STANDARD POSITIVE	GOLD STANDARD NEGATIVE
POSITIVE	TP	FP
NEGATIVE	FN	TN

TP : true positive
TN : true negative
FP : false positive
FN : false negative

Prior probability	the probability of disease before applying the test
Posterior probability	the probability of disease after the results of a test have been learned
Accuracy	overall agreement between the test and the golden standard. (TP+FN) : (TP+FP+TN+FN)
False negative proportion	the probability of a negative test-result when the disease is present. FN : (TP+FN) = 1-sensitivity
False positive proportion	the probability of a positive test-result with no disease present. FP : (FP+TN) = 1-specificity
Negative predictive value	probability of disease being absent when the test result is negative. TN : (TN+FN)
Positive predictive value	probability that necks diagnosed as having neck disease will indeed have metastatic nodes. TP : (TP+FN)
Prevalence	proportion of the truly diseased individuals to whom the test was applied. (TP+FN) : (TP+FP+TN+FN)

Sensitivity	ability of the test to detect the disease when it is present. TP : (TP + FP)
Specificity	ability of the test to identify the absence of disease. TN : (FP + TN)

Appendix D

Classification of nodal disease according UICC/AJC

The definitions of the N categories for all head and neck sites except the thyroid gland are:

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in a single homolateral lymph node, 3 cm or less in greatest dimension
N2a	Metastasis in a single homolateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension
N2b	Metastasis in multiple homolateral lymph nodes, none more than 6 cm in greatest dimension
N2c	Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension
N3	Metastasis in a lymph node, more than 6 cm in greatest dimension

Appendix E

Frequency of occult cervical metastases

I Very high frequencies of occult metastases are seen with carcinomas of the oropharynx, nasopharynx, and hypopharynx: up to 70%.[1 2 3 4 5 6 7]

II High frequencies of subclinical disease occur with T3,4 oral cavity and T3,4 supraglottic cancer: up to 54%.[3 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23]

III In T1,2 supraglottic, T1,2 soft palate and T3,4 glottic cancer the incidence may be 34%.[1 22 23 24]

IV Incidence is relatively low with T1,2 glottic, T1 oral, lower lip and any T-stage of sino-nasal cancer: up to 15%.[15 25]

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Summary

This thesis reports on the first five years of experience with ultrasound examination of the head and neck region in patients referred to the Department of Otorhinolaryngology and Head and Neck Surgery at the University Hospital Rotterdam. In a joint effort with the Department of Radiology, it was studied whether ultrasound examination could contribute to the following clinical problems:

- the fallibility of the current diagnostic tests to detect cervical nodal disease in patients with cancer of the upper aero-digestive tract; and,
- unsatisfactory current diagnostic tests to evaluate patients with palpable head and neck masses.

In Part I, general aspects of diagnostic ultrasound are introduced (chapter I.1 and I.2). At the start of our study, descriptions of the sonographic anatomy of the head and neck were not available. The ultrasound pattern of the structures which constitute the neck became clear in the course of the study. This pattern is described and illustrated in chapter I.3. In addition, the technique of ultrasound guided fine needle aspiration biopsy (UGFNAB) is outlined (chapter I.4).

In Part II, the value of pre-surgery ultrasound examination to detect cervical metastases was assessed by comparing the results of ultrasound to the findings of histopathological examination of neck dissection specimens. The sensitivity of ultrasound to identify metastatically involved necks appeared to be very high (97%) when compared to palpation (73%). The specificity however, was low (32%) since the images did not allow differentiation between benign and malignant nodes.
The technique of UGFNAB enabled identification of metastatic deposits in the non-palpable nodes which were detected by ultrasound. The accuracy of UGFNAB proved to be similar to that of conventional aspiration biopsy (chapter II.1 and II.2).
Multiplicity of nodal metastases and regional involvement were established with higher accuracy by ultrasound when compared to palpation and computed tomography (CT). For evaluation of patients at risk for retropharyngeal nodes, CT is indispensable (chapter II.3). It was concluded that ultrasound with UGFNAB is a reliable method for screening, demonstrating, and excluding nodal metastases. This combined procedure influenced the staging of patients with upper aero-digestive tract cancer considerably (chapter II.4).
The consequences of improved diagnostic acumen on clinical management are discussed in chapter II.5.

Head and neck masses may cause confusion in interpretation at clinical examination. In part III, the contribution of palpation and ultrasound examination to the diagnosis of these conditions are assessed. The ultrasound pattern of thyroglossal duct anomalies (chapter

III.1), branchiogenic cysts (chapter III.2), laryngoceles (chapter III.3), salivary gland disease (chapter III.4, III.5, and III.6) and cervical tuberculous adenitis (chapter III.7) is described. The differentiation between solid and cystic masses and the identification of the exact topographic relationships, permitted a correct ultrasound diagnosis in most of these patients. It was impossible to discern between the various types of salivary gland tumors on the basis of the ultrasound pattern. Cytologic examination appeared to be of significant value in this respect (chapter III.5).
In chapter III.9, the results and conclusions of the preceding chapters are summarized, and the values and limitations of ultrasound of the head and neck are discussed. It is concluded that ultrasound (with UGFNAB when required) may result in a more efficaceous work-up in patients with a head and neck mass. A guideline for the clinical use of ultrasound is presented in the addendum of Part III.

In Part IV, an alternative approach to the treatment of deep neck abscesses is presented. The technique of ultrasound guided percutaneous drainage, and the clinical course of 5 patients who were treated by this method are described.

In the final remarks, the subjective and interactive nature of diagnostic ultrasound is discussed. In addition, the low morbidity of ultrasound and cytologic examination are highlighted.

Samenvatting

Dit proefschrift is gebaseerd op de eerste 5 jaar ervaring met echografie van het hoofd-hals gebied bij patiënten verwezen naar de afdeling keel-, neus- en oorheelkunde van het Academisch Ziekenhuis Rotterdam. In nauwe samenwerking met de afdeling radiodiagnostiek werd onderzocht of echografie een bijdrage zou kunnen leveren aan de volgende twee klinische problemen:

- de lage nauwkeurigheid van de beschikbare diagnostische methoden om bij patiënten met een hoofd-hals maligniteit halskliermetastasen vast te stellen; en,
- onbevredigende diagnostische middelen voor onderzoek van patiënten met een zwelling in de hals.

Deel I bevat een introductie van enkele algemene aspecten van echografie (hoofdstuk I.1 en I.2). Gedurende de studie werd inzicht verkregen in de complexe echografische anatomie van de weke delen in het hoofd-hals gebied. Het echografisch beeld van deze structuren is beschreven en geïllustreerd in hoofdstuk I.3.
Voor nader onderzoek van de afwijkende structuren welke met echografie in beeld konden worden gebracht, werd een techniek voor echogeleide cytologische punctie ontwikkeld. Deze techniek is beschreven in hoofdstuk I.4.

Deel II betreft de waarde van palpatie, echografie, computer-tomografie (CT) en cytologie met betrekking tot het onderzoek naar halskliermetastasen bij patiënten met een plaveiselcelcarcinoom in het hoofd-hals gebied. In hoofdstuk II.1 zijn de bevindingen bij palpatie en echografie gecorreleerd aan histopathologisch onderzoek van halsklierdissectie preparaten. De sensitiviteit van echografie bleek hoog vergeleken met de sensitiviteit van palpatie (respectievelijk 97% en 73%). De specificiteit van echografie daarentegen was laag (32%), aangezien het niet mogelijk bleek op basis van het echografisch aspect onderscheid te maken tussen benigne klieren en metastasen. In hoofdstuk II.1 en II.2 werd onderzocht wat de waarde van de echogeleide cytologische punctie in dit opzicht zou kunnen zijn. Het onderscheid tussen reactieve lymfklieren en metastasen bleek met deze techniek betrouwbaar te maken, en de nauwkeurigheid van de methode bleek vergelijkbaar met cytologisch onderzoek van materiaal wat op conventionele wijze was verkregen (hoofdstuk II.2).
Het voorkomen van metastasen binnen een bepaalde regio van de hals, en multipliciteit van metastasen werden met behulp van echografie nauwkeuriger vastgesteld dan met palpatie en CT (hoofdstuk II.3).
Op basis van de hoge sensitiviteit van echografie en de betrouwbaarheid van echogeleide cytologische punctie is geconcludeerd dat echografie, gecombineerd met cytologie, een betrouwbare methode voor het opsporen, aantonen en uitsluiten van halskliermetastasen is.
Het effect van toepassing van deze diagnostiche methode op de stagering van patiënten met een hoofd-hals maligniteit is beschreven in hoofdstuk II.4.

De mogelijke consequenties voor het therapeutische beleid van de verbeterde diagnostiek van de hals worden bediscussieerd in hoofdstuk II.5.

In deel III wordt de bijdrage van echografie aan de diagnostiek van diverse zwellingen in het hoofd-hals gebied onderzocht. Het echografisch beeld van ductus thyreoglossus anomalieën (hoofdstuk III.1), laterale halscysten (hoofdstuk III.2), laryngocèlen (hoofdstuk III.3), speekselklierafwijkingen (hoofdstuk III.4, III.5 en III.6) en halskliertuberculose (hoofdstuk III.7) wordt beschreven en geïllustreerd. Op grond van het vermogen van echografie om onderscheid te maken tussen solide en cysteuze structuren, en het vermogen de exacte anatomische verhoudingen af te beelden, kon in veel gevallen een juiste diagnose gesteld worden.
Differentiatie van de verschillende histologische typen speekselkliertumoren met behulp van echografie was niet mogelijk. Cytologisch onderzoek bleek voor dit doel veel beter geschikt (hoofdstuk III.5).
De mogelijkheden en beperkingen van echografie zijn weergegeven in hoofdstuk III.9. De mogelijke plaats van echografie bij nader onderzoek van een zwelling in de hals e.c.i. wordt aangegeven.

In deel IV is een nieuwe methode voor behandeling van abcessen in de hals beschreven. De techniek en de resultaten van de behandeling bij 5 patiënten zijn genoemd.

In deel V wordt aandacht besteed aan het subjectieve karakter van diagnostische echografie. Verder worden de lage morbiditeit van echografie en cytologie belicht.

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